RETINAL NERVE FIBER LAYER MEASUREMENTS IN MYOPES AS DETERMINED BY OPTICAL COHERENCE TOMOGRAPHY

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ABSTRACT

BACKGROUND
Myopia is a common cause of visual disability throughout the world. One of the potentially blinding ocular diseases associated with myopia is glaucoma. Due to similar features of the optic disc in glaucoma and myopia, there may be a misdiagnosis of glaucoma in these individuals. Decrease in retinal nerve fiber layer (RNFL) thickness as measured by optical coherence tomography (OCT) is a sensitive indicator of early glaucomatous damage. However, it remains unclear if RNFL thickness varies with refractive status of the eye. We wanted to compare retinal nerve fiber layer thickness in low, moderate and high myopia patients and study the association between retinal nerve fiber layer thickness, axial length and myopic spherical equivalent.

METHODS
A total of 150 eyes of 150 subjects with varying degree of myopia presenting to the Department of Ophthalmology, Christian Medical College and Hospital, Ludhiana were included in the study group. Comprehensive ophthalmic examination was performed which included visual acuity, refraction by autorefractometer, axial length by NIDEK AL-SCAN and retinal nerve fiber layer thickness by optical coherence tomography (NIDEK RS 3000 LITE).

RESULTS
The average (360°) RNFL thickness was significantly lower in the high myopia group as compared to the low and moderate myopia groups (p < 0.0001). On quadrant wise analysis, the RNFL was thicker in the low myopia group than in the moderate and high myopia groups in the superior, nasal and inferior quadrants (p < 0.0001, p<0.0001 and p-0.0002 respectively). However, the RNFL thickness in the temporal quadrant was comparable in the three groups (p = 0.768).

CONCLUSIONS
Retinal nerve fiber layer thickness decreases as the spherical equivalent and axial length increases. Therefore, this profile should be taken into consideration while analysing RNFL thickness for glaucoma evaluation in subjects with highly myopia.

KEYWORDS
Myopia, Glaucoma, Retinal Nerve Fiber Thickness, Optical Coherence Tomography.

BACKGROUND
Myopia is the most common ocular abnormality world-wide. The World Health Organization has grouped myopia and uncorrected refractive error with cataract, macular degeneration, infectious disease and vitamin A deficiency among the leading causes of blindness and vision impairment in the world.[1]

The prevalence of myopia in adults has been reported to be 22.7% and 26.2% in the Baltimore Eye Survey and the Beaver Dam Study respectively.[2,3] According to epidemiological evidence, the prevalence of myopia is increasing, especially in Asian populations.[4] In population based studies, the prevalence of pathological myopia is estimated at 1-3%.[5]

One of the potentially blinding ocular diseases associated with myopia is glaucoma. The risk of developing glaucoma is two to three times higher in myopic individuals than in non-myopic individuals, and this risk is independent of other risk factors like high intraocular pressure.[6] Glaucoma is diagnosed by considering the appearance of the optic disc, RNFL and by standard achromatic perimetry. However, myopic individuals often have enlarged optic discs with a more oval configuration, larger areas of peripapillary atrophy, deformation of the optic discs, pale discs, shallow and large cups.[7] Due to these similar features, glaucomatous changes cannot be easily interpreted in myopic discs, possibly leading to a misdiagnosis of glaucoma.[8]

It is therefore important to investigate the correlation between RNFL measurements, axial length and refractive error in myopia in view of the observation that the risk of glaucoma increases with increasing degree of myopia. The

RNFL can be quantitatively assessed by the normative age matched database present in the optical coherence tomography (OCT). OCT is a non-contact and non-invasive modern imaging device based on coherence interferometry, which can directly measure and quantify RNFL thickness by calculating the area between the Internal Limiting Membrane (ILM) and RNFL border.[9] Newer versions of OCT based on spectral domain technology have been developed. This novel technique offers higher axial resolution and scanning speed than the conventional time domain techniques. The Stratus OCT provides detailed information and offers reduced test variability.

A need was felt to further evaluate the relationship between the axial length, myopia and RNFL thickness to avoid any wrong interpretation. Thus, this study was undertaken to assess the RNFL parameters in patients of myopia in our population.

METHODS

This was a prospective study conducted in the Department of Ophthalmology, Christian Medical College & Hospital, Ludhiana. A total of 150 eyes of 150 subjects with myopia were analysed. Informed consent was obtained from all subjects.

The subjects were divided into following groups of 50 eyes each -

Group A-Low myopes (-3.0< SE <-0.5 Dioptres (D))
Group B - Moderate myopes (-6.0< SE ≤ -3.0D)
Group C - High myopes (SE ≤ - 6.0D)
Spherical equivalent was calculated as sphere plus half negative cylinder.

Inclusion criteria were patients aged 15 to 60 years with myopia higher than -0.5D. Exclusion criteria were Ocular hypertension (IOP >21 mmHg), optic nerve head with glaucomatous damage, visual field defects, refractive surgeries or any intraocular surgery, diabetes mellitus, Hypertension, Peripapillary atrophy extending upto an area where OCT measurements are obtained normally, Cataract and media opacities.

If both eyes were eligible, the more myopic eye was selected and if spherical equivalent was equal in both eyes, then the right eye was included in the study.

Ocular Examination

All subjects underwent a complete ophthalmological examination including Visual Acuity (VA). Autorefractometer reading was taken and converted to spherical equivalents. Intra ocular pressure was measured by Goldmann Applanation Tonometer. Anterior segment examination was performed using a slit-lamp biomicroscope. Screening visual field examination using (24-2) Humphrey's Automated Visual Field Analyzer was done. The appearance of the optic nerve head was documented after dilating the pupils. The vertical disc diameter, cup-disc ratios and peripapillary atrophy were recorded.

Axial length was measured by NIDEK AL-SCAN optical biometer. It uses 830 nm super luminescent diode for axial length measurement with partial coherence interferometry.

Optical Coherence Tomography

OCT scanning was performed using Nidek-RS 3000 Lite. RNFL thickness measurements were obtained after pupil dilatation, using tropicamide 0.8% with phenylephrine hydrochloride 2.5%.

Three separate optic disc maps were acquired with NIDEK - RS3000 Lite. The RNFL thickness parameters evaluated in this study were temporal, superior, nasal and inferior quadrant thickness and the 360º average RNFL thickness. From the exported group of three scans, the most reliable scan was chosen for comparison (defined as the highest percentage of acceptable A-scan with the highest signal strength). The color code for each quadrant was noted. The colors white, green, yellow and red signified a >95%, 5-95%, 1-5% and <1% chance respectively, that the measured RNFL thickness was within normal range for an age matched population. The image was repeated if the subject moved or blinked during the scan. Scan was discarded and retaken if the signal strength was less than 6. Statistical analysis was done using SPSS software version 21. Significance levels was set at p <0.05.

RESULTS

In this study, a total of 150 eyes of 150 subjects with myopia who presented to the Department of Ophthalmology were included.

Demographic Details

Age of our subjects ranged from 18 years to 54 years with the mean age being 26.82 ± 8.184 years. The Mean age in the three groups was 26.72 ± 7.72, 27±8.41 and 26.74 ± 8.56 years respectively. Out of the 150 subjects enrolled in the study, 60 (40%) were men and 90 (60%) were women. The number of women was more in all the groups as compared to the men. However, there was no statistically significant difference in the age and gender distribution between the 3 groups. (Table 1 & 2).

Mean Axial Length and Spherical Equivalent

The mean axial length in the three groups was 23.94 ± 0.78 mm, 24.87 ± 0.81 mm and 25.95 ± 1.03 mm respectively. The difference was found to be statistically significant (p <0.001). The spherical equivalent values in the three groups were -1.86 ± 1.13D, -4.37 ± 0.84D, -7.96 ± 2.1D respectively. There was a statistically significant difference in the spherical equivalent between the three groups as well (p < 0.0001). (Table 3).

RNFL Thickness Measurements

The average (360°) RNFL thickness was significantly lower in the high myopia group (96.3 ± 10.94 µm) as compared to the low (107.32 ± 6.85 µm) and moderate myopia groups (101.54 ± 6.97 µm) (p < 0.0001) (Table 4).

On quadrant wise analysis, the RNFL was thicker in the low myopia group than in the moderate and high myopia groups in the superior, nasal and inferior quadrants and this difference was statistically significant (p < 0.0001, p<0.0001 and p-0.0002 respectively). However, the RNFL thickness in the temporal quadrant was comparable in the three groups (p = 0.768) (Table 4).

Correlation Between RNFL Thickness and Axial Length

The correlation coefficients were determined between the RNFL thickness (average and quadrant wise) and the mean axial length. There was a negative correlation between RNFL thickness (average 360 degrees) and axial length (r-0.415, p < 0.0001) (Table 5).

	Low Myopia (n = 50)	Moderate Myopia (n = 50)	High Myopia (n =50)	p Value
Age (years) Mean ± SD	26.72 ± 7.72	27 ± 8.41	26.74 ± 8.56	0.845

Table 1. Mean Age Distribution Between the Mild, Moderate and High Myopes

Gender	Mild Myopia (n=50)	Moderate Myopia (n=50)	High Myopia (n=50)	Total	p Value
Male	22 (44%)	23 (46%)	15 (30%)	60 (40%)	p = 0.205
Female	28 (56%)	27 (54%)	35 (70%)	90 (60%)	

Table 2. Gender Distribution in the 3 Groups

	Low Myopia (n = 50)	Moderate Myopia (n = 50)	High Myopia (n = 50)	p Value
Axial length (mm)	23.94 ± 0.78	24.87 ± 0.81	25.95 ± 1.03	< 0.0001
Spherical equivalent (D)	-1.86 ± 1.13	-4.37 ± 0.84	-7.96 ± 2.1	< 0.0001

Table 3. Axial Length and Spherical Equivalent Measurements in the 3 Groups

RNFL Thickness (µm)	Low Myopia (n=50)	Moderate Myopia (n=50)	High Myopia (n=50)	p Value
Average (360°)	107.32 ± 6.85	101.54 ± 6.97	96.3 ± 10.94	< 0.0001
Superior	131.44 ± 15.25	125.26 ± 13.03	13.16 ± 16.73	< 0.0001
Inferior	136.84 ± 12.43	127.02 ± 12.65	118.7 ± 16.42	< 0.0001
Nasal	86.94 ± 9.95	79.7 ± 10.33	77.54 ± 14.31	0.0002
Temporal	70 ± 9.3	70.14 ± 12.13	70.8 ± 13.26	0.768

Table 4. Retinal Nerve Fiber Layer Thickness in the 3 Groups

RNFL Thickness (µm)	Axial length (n=150)	
	R	p
Average (360°)	- 0.415	<0.0001
Superior	- 0.4	<0.0001
Inferior	- 0.439	<0.0001
Nasal	- 0.325	<0.0001
Temporal	0.119	0.1462

Table 5. Correlation Analysis Between RNFL Measurements and Axial Length

r= Pearson correlation coefficient.

Correlation Between RNFL Thickness and Spherical Equivalent

The correlation coefficients were determined between the RNFL thickness (average and quadrant wise) and the mean spherical equivalent. The RNFL thickness (average, superior, inferior and nasal) showed a positive correlation with the spherical equivalent which was also statistically significant (p < 0.0001). However, temporal quadrant showed a negative correlation with the spherical equivalent, but it was statistically insignificant (p = 0.5937). Thus, an increase in spherical equivalent (more negative) was associated with a corresponding decrease in the RNFL thickness in all quadrants except temporal (Table 6).

RNFL Thickness (µm)	Spherical Equivalent (n=150)	
	R	p
Average 360^0	0.484	< 0.0001
Superior	0.474	< 0.0001
Inferior	0.495	< 0.0001
Nasal	0.327	< 0.0001
Temporal	-0.044	0.5937

Table 6. Correlation Analysis Between RNFL Thickness and Spherical Equivalent

DISCUSSION

In our study, the average (360°) RNFL thickness was significantly lower in the high myopia group (96.3 ± 10.94 µm) than in the low (107.32 ± 6.85 µm) and moderate myopia groups (101.54 ± 6.97 µm) (p < 0.0001).

In a study conducted by Kamath et al in 118 myopes, the average RNFL thickness was lower in the high myopia group (80.45 ± 10.1 µm) than in the low (94.9 ± 7.8 µm) and moderate myopia groups (87.1 ± 10.8 µm).[10] In a similar study from China by Zha et al on 271 subjects, the average RNFL thickness was lower in high myopia group (90.57 ± 10.07 µm) than in low (101.46 ± 7.95 µm) and moderate myopia group (99.15 ± 8.94 µm).[11] The average RNFL thickness in all three groups in these studies were less than ours, but the differences between the three were similar. Kim et al measured peripapillary RNFL thickness in 48 myopic subjects using Stratus OCT. The global average RNFL thickness (107.4 ± 7.6 µm) was found to be significantly thinner in the high myopia group than in the low myopia (115.8 ± 8.5 µm) and moderate myopia group (112.2 ± 10.0 µm).[12]

On quadrant wise analysis, the current study found that RNFL thickness was more in the low myopia group than in the moderate and high myopia groups in the superior, inferior and nasal quadrants (p < 0.0001, p < 0.0001 and p - 0.0002 respectively). However, the RNFL thickness in the temporal quadrant was thicker in high myopia compared to low and moderate myopia groups (p = 0.768). Similarly, in a study conducted by Kamath et al in 118 myopes, the RNFL thickness was found to be more in the low myopia group than moderate and high myopia group in the superior, inferior and nasal quadrants (p ≤ 0.020). However, temporal quadrant showed thinning in low myopia group than in moderate and high myopia groups (p < 0.98).[10]

In another study done by Kim et al, the RNFL thickness was found to be more in the superior, inferior and nasal quadrant (p = 0.020, p < 0.001 and p < 0.001 respectively) in the low myopia group when compared to the moderate and high myopia groups. The RNFL thickness in the temporal quadrant was more in the moderate and high myopia groups as compared to the low myopia group (p = 0.001).[12]

Wang et al assessed quadrant wise RNFL thickness in 149 myopes. They also found significant decrease in superior and inferior quadrants (p = 0.002 and p <0.001 respectively), statistically insignificant change in nasal quadrant (p = 0.255) and thickening in the temporal quadrant (p = 0.166) in high and moderate myopia groups than low myopia group.[13]

The thicker RNFL values found in the temporal quadrant in all the above studies including ours, despite the lower 360^0 average RNFL thickness among subjects with highly myopic eyes, suggests that a redistribution of the RNFL might occur as the axial length gets longer. Kim et al speculated that as the axial length increases, the retina is dragged toward the temporal horizon. In this process, the RNFL layers are compressed against the bundles originating from the opposite hemisphere at the horizontal raphe. This results in thickening of the RNFL in the temporal quadrant. In contrast, the nasal retina becomes thinner as it is stretched. The possibility of such retinal 'dragging' toward the horizontal raphe is supported by the closer locations of the superior and inferior peak RNFL thickness to the temporal horizon.[12]

Kim et al recognized that the actual scanning radius in eyes with greater axial length (myopic eyes) could be longer than 1.7 mm due to the magnification effect. Thus, the comparison of the RNFL thickness between the high myopic eyes and low myopic eyes using the same sized scan circle might be misleading because the RNFL thickness decreased at increasing distances from the optic disc. However, the potential larger diameter of the scan circle in high myopic eyes did not necessarily mean that the RNFL was being measured farther from the disc margin in high myopic eyes. It may be because the optic disc size may also increase with myopia.[12]

In the present study, there was a negative correlation between average RNFL thickness and axial length (r = - 0.415, p <0.0001). On quadrant wise analysis also, a negative correlation was seen between the superior, inferior and nasal quadrants (r = - 0.4, r = - 0.439 and r = - 0.325 respectively) and axial length (p<0.001). However, the temporal quadrant showed a positive correlation with axial length, but it was statistically insignificant (r = 0.119, p = 0.1462).

Wang et al also showed a negative correlation between average RNFL thickness and axial length (r = - 0.32, p <0.001). In quadrant wise analysis also, their results were comparable to our study. They showed a negative correlation between the superior (r = - 0.34, p <0.001), inferior (r= - 0.43, p <0.001) and nasal quadrants (r = - 0.11, p = 0.180). However, the temporal quadrant showed

a positive correlation with axial length (r = 0.23, p = 0.005).[13]

Zhao et al showed similar results to our study, where they found a negative correlation with average RNFL thickness and axial length (r = - 0.33, p <0.001). On quadrant wise analysis, a negative correlation was seen between the superior (r = - 0.20, p = 0.001), inferior (r = - 0.37, p <0.001), nasal quadrants (r = - 0.30, p <0.001) and axial length. However, the temporal quadrant showed a positive correlation with axial length (r = 0.13, p = 0.019).[14] Thus, an increase in axial length was associated with a corresponding decrease in the average RNFL thickness as well as decrease in the superior, inferior and nasal quadrant. For every 1 mm increase in axial length, RNFL thickness decreased by 3.38 μm. Similarly, for every 1D increase in myopia (more negative), RNFL thickness decreased by 1.59 μm.

In contrast, Hoh et al conducted a study on 132 myopes, where mean peripapillary RNFL thickness did not correlate with axial length for the 3.40 mm scan diameter (r = - 0.04, p = 0.62), 4.50 mm scan diameter (r = 0.03, p = 0.75) or variable scan diameter set at 1.75 × VDD (vertical disc diameter) (r = - 0.02, p = 0.78). They suggested that the peripapillary RNFL thickness does not vary with the axial length.[15]

These differences can be attributed to the different OCT imaging equipment used. Hoh et al used OCT 1 (first generation), which obtains only 12 RNFL thickness values from each scan, while the other studies, including ours, used spectral domain OCTs. It is likely that the values obtained in OCT 1 scans may be insufficient to pick up difference due to axial length or degree of myopia.

del - Rosario et al studied the correlation between RNFL thickness and spherical equivalent. They found a positive correlation between average RNFL thickness and spherical equivalent (r = 2.868, p = 0.036). On quadrant wise analysis, they found a positive correlation between the aforementioned parameters in the superior quadrant (r = 3.258, p = 0.126), inferior quadrant (r = 6.277, p = 0.007) and nasal quadrant (r = 3.370, p = 0.024). There was a negative correlation between RNFL thickness in the temporal quadrant and spherical equivalent (r = -1.555) which was statistically insignificant (p < 0.641).[16]

Wang et al reported a positive correlation between average RNFL thickness and spherical equivalent (r = 0.29, p <0.001). They also showed a positive correlation between RNFL thickness in superior (r = 0.32, p<0.001) inferior (r = 0.37, p<0.001), nasal quadrants (r = 0.10, p= 0.210) and negative correlation with temporal quadrant and spherical equivalent (r = - 0.20, p=0.016).[13]

Compared to the above studies, the present study showed a positive correlation between the RNFL thickness (average 360°, superior, inferior and nasal) and spherical equivalent which was also statistically significant (p < 0.0001). However, temporal quadrant showed a negative correlation with the spherical equivalent, but it was statistically insignificant (p = 0.5937). Thus, an increase in spherical equivalent (more negative) was associated with a

corresponding decrease in the RNFL thickness in all except temporal quadrant.

In contrast, in the study done by Hoh et al the mean peripapillary RNFL thickness did not correlate with spherical equivalent for the 3.40 mm scan diameter (r = - 0.11, p = 0.22), 4.50 mm scan diameter (r = - 0.103, p = 0.24) or variable scan diameter set at 1.75 × VDD (r = -0.08, p = 0.36).[15] They suggested that the peripapillary RNFL thickness does not vary with spherical equivalent. Again, these differences could be attributed to the different OCT imaging equipment used.

CONCLUSIONS

It was seen that the retinal nerve fiber layer thickness decreases as the spherical equivalent and axial length increases. Therefore, this profile should be taken into consideration while analysing RNFL thickness in subjects with highly myopic eyes, when aiming to diagnose glaucoma.

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