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COMPARING RETINAL NERVE FIBER LAYER THICKNESS IN MYOPIA WITH CONTROLS IN A TERTIARY CARE CENTRE IN NORTH INDIA

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ABSTRACT **INTRODUCTION:** To compare the peripapillary retinal nerve fiber layer (RNFL) thickness measured via optical coherence tomography (OCT) between different groups of myopia severity and controls.

METHODS: This was a prospective cross-sectional study. All subjects underwent a full ophthalmic examination, refraction, visual field analysis and A-scan biometry. Myopic patients were classified as low myopia (LM), moderate myopia (MM) and high myopia (HM). The control group consisted of emmetropic (EM) patients. A Zeiss Cirrus HD-OCT machine was used to measure the peripapillary RNFL thickness of both eyes of each subject. The mean peripapillary RNFL thickness between groups was compared using both analysis of variance and analysis of covariance.

RESULTS: A total of 322 eyes of 322 subjects were included in this study. Approximately two-thirds were female (n=204). The mean age was 30.68±10.6y. There were 144 (44.7%) eyes with EM, 99 (30.8%) eyes with LM, 58 (18%) eyes with MM and 21(6.5%) eyes with HM. All groups of myopia severity had a thinner average RNFL than the EM group, but after controlling for gender, age, and axial eye length, only the HM group differed significantly from the EM group (P=0.017). Likewise, the superior, inferior and nasal RNFL was thinner in all myopia groups compared to controls, but after controlling for confounders, only the inferior quadrant RNFL was significantly thinner in the HM group, when compared to the EM group (P=0.017).

CONCLUSION: The average and inferior quadrant RNFL is thinner in highly myopic eyes compared to emmetropic eyes. Refractive status must be taken into consideration when interpreting the OCT of myopic patients, as RNFL thickness varies with the degree of myopia.

KEYWORDS : optical coherence tomography; retinal nerve fiber layer; myopia

INTRODUCTION

In the past decades the prevalence of myopia has been increasing, with nearly half of the world population predicted to be myopic by 2050[1-2]. It is very common condition in Asia, where the prevalence has been estimated to be as high as 90% in East Asia [3-4]. Other eye diseases are associated with myopia, of which glaucoma remains one of the pertinent [5-6]. The morphological appearance of the optic nerve head in myopia renders the clinical diagnosis and monitoring of glaucoma progression in myopic eyes challenging, especially as these eyes may have concomitant visual field defects mimicking those seen in glaucoma [7]. Optical coherence tomography (OCT) can aid in the diagnostic dilemma by measuring retinal nerve fiber layer (RNFL) thickness, which differs significantly between glaucoma patients and controls[8-11]. However, myopic patients may have RNFL abnormalities which may complicate this interpretation. Our study aimed to compare peripapillary RNFL thickness between different groups of myopia severity and controls using Zeiss Cirrus HD-OCT.

MATERIALS AND METHODS

This was a prospective cross-sectional study conducted in the Department of Ophthalmology in SMHS hospital, a tertiary hospital in Srinagar, Kashmir. The study was approved by the Ethical committee of the hospital. Inclusion criteria were adults aged 18 to 60 years of age with no ocular pathology. We excluded those with a history of previous ocular trauma or surgery. Those with a cup-disc ratio greater than 0.7, an intraocular pressure greater than 21 mm Hg, visual field abnormalities, a first degree family member with glaucoma were also excluded. All subjects underwent a full ophthalmic examination, including distance Snellen visual acuity, refraction, slit-lamp biomicroscopy of the anterior segment, assessment of intraocular pressure by Goldmann applanation tonometry and dilated fundus examination. Myopic patients were classified based on their spherical equivalent (SE).

The severity groups were as follows: low myopia (LM; SE greater than -0.5 D, up to -3.0 D), moderate myopia (MM; SE greater than -3.0 D, up to -6.0 D) and high myopia (HM; SE greater than -6.0 D)[12]. The control group was emmetropia (EM), defined as a SE from +0.5 D to -0.5 D. Other examinations included visual field (SITA fast 24-2 Humphrey Field Analyser II, Carl Zeiss Meditec, Germany) and A-scan biometry (PAC SCAN 300 A Sonomed Digital Biomedic Ruler). Cirrus HD-OCT (Carl Zeiss Meditec, Inc. Germany) was used to

measure the peripapillary RNFL thickness of both eyes of each subject. This was a spectral-domain OCT device with an acquisition rate of 27 000 A-scans per second. After the subject was properly seated, the iris was brought into view using the mouse-driven alignment system. The line scanning ophthalmoscopic image was focused, and the optic nerve head centered in the viewer. The software's automated built-in algorithms identified the center of the optic disc, and a circle measuring 3.46 mm in diameter was positioned automatically evenly around the disc center to generate average, quadrant and clock-hour peripapillary RNFL measurements. A satisfactory scan required optic disc centration, images in clear focus and signal strength of ≥6. Images with movement artifact or signal strength of less than 7 were repeated once, if the second scan was also unusable, the eye was excluded from the study. The peripapillary RNFL parameters evaluated in this study consisted of mean 360°,superior, inferior, nasal and temporal quadrant thickness. The mean peripapillary RNFL thickness between groups was compared using both analysis of variance (ANOVA) and analysis of covariance (ANCOVA) to control for potential confounders.

RESULTS

A total of 322 eyes of 322 subjects were included in this study. Approximately two-thirds were female (n=204). The mean age was 30.68±10.6y. There were 144 (44.7%) eyes with EM, 99 (30.8%) eyes with LM, 58 (18%) eyes with MM and 21(6.5%) eyes with HM (Table 1).

Table 1 Age, axial length and 360° RNFL thickness in EM, LM, MM and HM groups

Variable	EM	LM	MM	HM
Age (y)	31.35±10.4	31.02±9.6	31.18±10.9	31.03±8.4
Axial length (mm)	23.08±0.78	23.69±0.74	25.03±0.82	26.22±1.14
Average RNFL thickness(μm)	100.6±9.8	98.56±8.44	94.87±8.87	89.64±9.26

EM: Emmetropia; LM: Low myopia; MM: Moderate myopia; HM: High myopia.

A significant inter-group difference for all RNFL parameters was observed (Table 2). Myopic groups had a thinner average RNFL than the EM group, and their RNFL was thinner in all quadrants except temporally.

Table 2   RNFL thickness and axial length in EM, LM, MM and HM groups

Variable	EM (n=144)	LM (n=99)	MM (n=58)	HM (n=21)	$P
360o average RNFL thickness (μm)	100.6±9.8	98.56±8.44	94.87±8.87	89.64±9.26	<0.001
Superior quadrant RNFL thickness (μm)	128.33±16.89	126.29±15.84	117.88±15.28	109.85±14.94	<0.001
Inferior quadrant RNFL thickness (μm)	133.78±16.88	128.51±16.34	121.03±15.24	109.66±15.02	<0.001
Nasal quadrant RNFL thickness (μm)	68.46±10.42	66.83±9.72	62.92±9.04	62.89±9.68	<0.001
Temporal quadrant RNFL thickness (μm)	70.22±9.56	71.67±11.98	75.87±14.08	75.65±14.79	<0.001
Axial length (mm)	23.08±0.78	23.69±0.74	25.03±0.82	26.22±1.14	<0.001

EM: Emmetropia; LM: Low myopia; MM: Moderate myopia; HM: High myopia. $ANOVA was applied

The myopic groups had a thinner average RNFL than the emmetropic group, with a statistically significant difference observed only between the HM and the EM group, after controlling for age, gender and axial length of the eye (P=0.017; Table 3). The mean inferior quadrant RNFL was significantly thinner in the HM group compared to the EM group, after adjustment for above mentioned factors (P=0.017; Table 4). There were no statistically significant differences of RNFL thickness among groups in the superior, nasal and temporal quadrants, after adjustment for confounders.

Table 3: Comparison of average RNFL thickness between EM, LM, MM and HM groups

Refractive Error Groups	Adjusted Mean (95% CI)	1Adjusted Mean difference (95%CI)	aP
EM/LM	99.02 (97.35, 100.70)/97.17 (95.30, 99.03)	1.85 (-1.00, 5.11)	0.450
EM/MM	99.02 (97.35, 100.70)/95.09 (92.45, 97.73)	3.93 (-0.34, 8.61)	0.088
EM/HM	99.02 (97.35, 100.70)/91.10 (86.41, 95.79)	7.92 (0.96, 15.28) 0.017	0.017
LM/MM	97.17 (95.30, 99.03)/95.09 (92.45, 97.73)	2.08 (-2.06, 6.22)	1.000
LM/HM	97.17 (95.30, 99.03)/91.10 (86.41, 95.79)	6.07 (-0.60, 12.73)	0.098
MM/HM	95.09 (92.45, 97.73)/91.10 (86.41, 95.79)	3.99 (-2.02, 9.99)	0.477

EM: Emmetropia; LM: Low myopia; MM: Moderate myopia; HM: High myopia; CI: Confidence interval. 1ANCOVA was applied, aP<0.05 is statistically significant.

Table 4: Comparison of mean inferior quadrant RNFL thickness between EM, LM, MM and HM groups

Refractive error groups	Adjusted mean (95%CI)	1Adjusted mean difference (95%CI)	aP
EM/LM	130.43 (127.77, 133.70)/126.15 (123.15, 129.75)	3.98 (-1.12, 9.69)	0.217
EM/MM	130.43 (127.77, 133.70)/123.83 (119.16, 128.50)	6.60 (-1.01, 14.82)	0.127
EM/HM	130.43 (127.77, 133.70)/116.42 (108.13, 124.71)	14.01 (1.65, 26.97)	0.017
LM/MM)	126.15 (123.15, 129.75)/123.53 (119.16, 128.50	2.62 (-4.70, 9.94)	1.000
LM/HM	126.15 (123.15, 129.75)/116.42 (108.13, 124.71)	9.73 (-1.76, 21.82)	0.148
MM/HM)	123.53 (119.16, 128.50)/116.42 (108.13, 124.71	7.11 (-3.22, 18.04)	0.392

EM: Emmetropia; LM: Low myopia; MM: Moderate myopia; HM: High myopia; CI: Confidence interval. 1ANCOVA was applied; aP<0.05 is statistically significant.

DISCUSSION

Researchers have been trying to identify risk factors for myopia[13-16] as well as the optimal management of the disease and its complications[17-19]. HM, especially, is associated with both maculopathy and glaucomatous optic neuropathy, rendering OCT an indispensable imaging modality in such patients[20-21]. Our study provides mean RNFL values of Zeiss Cirrus HD-OCT and demonstrates significant RNFL thickness differences between myopic patients and controls.

We observed that the mean RNFL thickness was significantly lower in highly myopic eyes compared to emmetropic eyes. This is in agreement with similar studies performed using RTVue-100 and Fourier domain OCT[22-23]. Although increasing axial length has been associated with RNFL thinning[24-25], we observed that the extent of this thinning was not statistically significant between the highly myopic group and other groups. Our findings are in contrast to those of Sezgin Akcay et al[26] and Kim et al[27], who observed that patients with HM have a thinner average RNFL than those with low and moderate myopia. Inter-group comparison of RNFL quadrant thickness revealed that the RNFL thinning seen in highly myopic eyes was not uniformly distributed; significant thinning was observed in the inferior quadrant RNFL of highly myopic eyes. However, our study failed to observe any significant inter-group differences in RNFL thickness of the superior and nasal quadrants. These findings are in inverse correlation to the two studies cited above[26-27], which observed that the RNFL was thicker in the LM group than in the moderate and/or HM groups for the superior, nasal and inferior quadrants.

The differences between our study and those cited may be due to the effect of confounders such as age[28-29], as multivariate analysis was not applied in the aforementioned studies. Reduced thickness of the middle to inner retina in myopia leads to retinal thinning , which has been correlated functionally to reduced spatial resolution[30]. This thinning has been explained by stretching of the ocular layers during eyeball elongation, as occurs in pathologic myopia[31]. Increased axial length has also been associated with narrowed retinal arterioles [32-33] and decreased peripapillary retinal flow perfusion. Whether these vascular changes precede or follow the RNFL thinning is still a matter of debate[34].

Strengths of our study include a relatively large sample size,adjustment for confounders and the elimination of inter-observer errors by using a single operator to perform refraction, ocular biometry and OCT of the RNFL. But unequal number of samples in each refractive error group, with the highly myopic group comprising the smallest proportion is the limitation of our study. In addition, we could have inadvertently introduced selection bias when we excluded subjects with abnormal visual fields and increased cup disc ratio. We did not adjust for magnification effect, which may also potentially affect the measured RNFL thickness[35]. Despite these limitations, our study clearly demonstrates that highly myopic eyes have a thinner RNFL than normal eyes. This thinning may be a risk factor for glaucoma development, as variations in the arrangement of optic nerve head fibers have been postulated to render myopic eyes more susceptible to glaucomatous damage[5,36].

CONCLUSIONS

While evaluating peripapillary RNFL thinning in myopic eyes, the clinician must bear in mind that the age-matched normogram provided by the software to guide RNFL thickness assessment may not be valid, as it does not contain algorithms to adjust for axial length and refractive error. Highly myopic eyes have thinner average and inferior quadrant RNFL compared to emmetropic eyes. Thus interpretation of RNFL thickness in highly myopic eyes should be performed with caution.

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