Association of Retinal Nerve Fiber Layer Thickness and Degree of Myopia Using Spectral Domain Optical Coherence Tomography

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ABSTRACT

Background: High myopia is defined as refractive error above -6.0 D and axial length above 26 mm. High myopia and its complications are considered to be one of the most significant causes of blindness and visual impairment in young people.

Objective: To evaluate the effect of the degree of myopia on the peripapillary retinal nerve fiber layer (RNFL) thickness by spectral-domain optical coherence tomography (OCT).

Patients and Methods: The study had been carried out in Embaba Ophthalmic Hospital during the period of June 2018 to February 2019. The study included 60 eyes, divided equally into 3 groups: **Group A:** Mild myopia (spherical equivalent between −0.5 and −3.0 D). **Group B:** Moderate myopia (spherical equivalent between −3.1 and −5.99 D). **Group C**: High myopia (spherical equivalent more than −6.0 D).

Results: This study showed that RNFL thickness was lower in the high and moderate myopic eyes compared with low myopic eyes in all quadrants except in temporal quadrant. A highly significant positive correlation was evident between spherical equivalent and RNFL thickness in each quadrant. A highly significant negative correlation between axial length and RNFL thickness was found in each quadrant.

Conclusion: High myopia should be considered in the interpretation of OCT data because of thinning of RNFL thickness and normative database corrected for refractive error and axial length should be incorporated. It is difficult for OCT to discriminate between high myopes with and without glaucoma. Therefore, clinical signs of glaucomatous nerve fiber damage are very important.

Keywords: Myopia, Retinal Nerve, Fiber Layer Thickness, Optical Coherence Tomography

INTRODUCTION

Myopia and its ocular morbidity represent a major concern regarding its clinical and socioeconomic perspectives considering its high prevalence and increasing rate. High myopia defined as refractive error more than −6.00 D and axial length more than 26 mm, is among the leading causes of visual impairment in young population **(1)**. Among its potential morbidity, myopia was proposed to be a risk for glaucoma **(2)**.

Myopic eyes are at a two-three times higher risk of developing glaucoma than emmetropic eyes **(3)**.

Nevertheless, this relationship remains obscure. Retinal nerve fiber layer (RNFL) thickness is an important parameter to follow the extent of glaucomatous damage **(4)**.

However, it remains uncertain whether RNFL thickness varies with the refractive state of the eye or not. Therefore, it is important to investigate whether any correlation exists between RNFL thickness and axial length or refractive state of the eye **(5)**.

Several explanations for RNFL thinning in myopia were reported. Myopic globe elongation may serve to stretch and thin the RNFL because of mechanical forces **(6)**.

Optical coherence tomography (OCT) is an essential tool for noninvasive in vivo analysis of retinal tissue for diagnosis and management of retinal disease and glaucoma. This technique is based on the degree of absorption or dispersion of light traversing the tissue. The light, which is divided into a detection arm and a reference arm, is emitted by a super luminescent diode at a wavelength of approximately 840 nm **(7)**.

Optical coherence tomography (OCT) is an objective and accurate method for RNFL thickness measurement. Compared with other RNFL analyzers, such as scanning laser polarimetry and Heidelberg retinal tomography, OCT provides high-resolution images with a quantitative analysis of the retinal features. With the recent technology of spectral-domain (SD) - OCT, ultra-high resolution three- dimensional images of the retina and optic disc can be obtained with ultra-high speed **(8)**.

AIM OF THE WORK

To evaluate the effect of the degree of myopia on the peripapillary retinal nerve fiber layer thickness by spectral-domain optical coherence tomography.

PATIENTS AND METHODS

The study had been carried out in Embaba Ophthalmic Hospital during the period of June 2018 to February 2019.

The study included 60 eyes, divided equally into 3 groups:

1. **Group A:** Mild myopia (spherical equivalent between −0.5 and −3.0 D)
2. **Group B:** Moderate myopia (spherical equivalent between −3.1 and −5.99 D).

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3. **Group C**: High myopia (spherical equivalent more than −6.0 D).

Ethical consideration and written informed consent:

An approval of the study was obtained from Al-Azhar University Academic and Ethical Committee.

Every patient signed an informed written consent for acceptance of the operation after explanation of the benefits of the procedure.

Inclusion criteria:

- Age between 20 and 55 years old.
- Spherical equivalent more than −0.5.

Exclusion criteria:

- Intraocular pressure more than 21 mmHg.
- Ocular media opacities.
- Abnormal optic disc (e.g., tilted disc or peripapillary atrophy).
- Previous intraocular surgery.
- Systemic diseases such as diabetes mellitus, or coexisting retinal disease.

Methods:

Patients included in the study were subjected to:

- **Full history taking.**
- **Ophthalmological examination:**
  1. Visual acuity assessment using auto refractometer refraction and best corrected visual acuity assessment using Snellen chart.
  2. Slit lamp examination of anterior segment.
  3. Intraocular pressure measurement by Goldmann applanation tonometry.
  4. Fundus examination using slit lamp biomicroscopy with +90 diopter lens.
- **Axial length measurement**: was measured using IOL master 700.
- **Peripapillary RNFL thickness**: was measured in each quadrant using spectralis OCT device (Heidelberg Engineering, Dossenheim, Germany)

Statistical analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA 2015). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

- A one-way analysis of variance (ANOVA) when comparing between means of the 3 groups.
- Post-hoc test: Least significant difference (LSD) was used for multiple comparisons between different variables.
- Chi-square (X^2) test of significance was used in order to compare proportions between qualitative parameters.
- The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:
  – P-value ≤0.05 was considered significant.
  – P-value <0.001 was considered as highly significant.
  – P-value >0.05 was considered insignificant.

RESULTS

Age of patients range was 20-55 years. The basic charterers of the patients are listed in table 1.

Table (1): Baseline characteristics distribution of the study group.

Baseline characteristics	Total (n=60)
Age (years) *Mean±SD*	34.86±7.15
Sex Male Female	 32 (53.3%) 28 (46.7%)
Spherical equivalent	-5.28±3.10
Axial length	26.40±0.41 mm

The study shows no statistically significant difference between studied groups according to demographic data **(Table 2).**

Table (2): Comparison between studied groups according to demographic data.

Demographic data	Group A: Low myopia (*N*=20)	Group B: Moderate myopia (*N*=20)	Group C: High myopia (*N*=20)	P-value
Age (years) *Mean±SD*	32.90±6.24	35.79±7.91	33.89±7.31	>0.05
Sex Male Female	 11 (55%) 9 (45%)	 11 (55%) 9 (45%)	 10 (50%) 10 (50%)	>0.05

The study shows highly statistically significant difference between studied groups according to spherical equivalent **(Table 3).**

Table (3): Comparison between studied groups according to spherical equivalent

Spherical equivalent	**Group A: Low myopia (*N*=20)**	**Group B: Moderate myopia (*N*=20)**	**Group C: High myopia (*N*=20)**	**p-value**
Mean±SD	-1.80±0.75	-4.66±0.84	-9.38±1.71	<0.001**

***p-value <0.001 HS*

The study shows highly statistically significant difference between studied groups according to axial length **(Table 4).**

Table (4): Comparison between studied groups according to axial length

Axial length	**Group A: Low myopia (*N*=20)**	**Group B: Moderate myopia (*N*=20)**	**Group C: High myopia (*N*=20)**	**p-value**
Mean±SD	25.24±0.30 mm	26.06±0.37 mm	27.91±0.57 mm	<0.001**

***p-value <0.001 HS*

The study shows statistically significant difference between studied groups according to retinal nerve fiber layer thickness **(Table 5).**

Table (5): Comparison between studied groups according to retinal nerve fiber layer thickness

Retinal nerve fiber layer thickness	**Group A: Low myopia (*N*=20)**	**Group B: Moderate myopia (*N*=20)**	**Group C: High myopia (*N*=20)**	**p-value**
Superior	117.10±5.95 µm	100.80±6.29 µm	94.86±6.12 µm	<0.001**
Inferior	129.13±5.10 µm	108.22±6.23 µm	101.80±5.91 µm	<0.001**
Nasal	70.15±5.09 µm	60.98±5.63 µm	55.73±5.97 µm	<0.001**
Temporal	79.52±4.61 µm	82.00±5.25 µm	78.63±5.90 µm	>0.05
Average	100.10±5.70 µm	86.80±5.20 µm	83.41±6.21 µm	<0.001**

***p-value <0.001 HS*

The study shows positive significant correlation between spherical equivalent with retinal nerve fiber layer thickness of the study group **(Table 6).**

Table (6): Correlation between spherical equivalent with retinal nerve fiber layer thickness of the study group

Retinal nerve fiber layer thickness	**Spherical equivalent**	
	r	**p-value**
Superior	0.843	<0.001**
Inferior	0.790	<0.001**
Nasal	0.831	<0.001**
Temporal	0.557	<0.001**
Average	0.722	<0.001**

***p-value <0.001 HS*

The study shows negative significant correlation between spherical equivalent with retinal nerve fiber layer thickness of the study group **(Table 7).**

Table (7): Correlation between axial length with retinal nerve fiber layer thickness of the study group

Retinal nerve fiber layer thickness	**Axial length**	
	r	**p-value**
Superior	-0.831	<0.001**
Inferior	-0.720	<0.001**
Nasal	-0.830	<0.001**
Temporal	-0.558	<0.001**
Average	-0.711	<0.001**

***p-value <0.001 HS*

DISCUSSION

The present study showed that RNFL thickness was lower in the high and moderate myopic eyes compared with low myopic eyes in all quadrants except in temporal quadrant. A highly significant positive correlation was evident between spherical equivalent and RNFL thickness in each quadrant. A highly significant negative correlation between axial length and RNFL thickness in each quadrant.

The RNFL measurements were lower in the high and moderate myopic eyes compared with low myopic eyes in all quadrants ($P<0.001$) except in temporal quadrant ($P>0.05$) which was not affected by degree of myopia. Average RNFL thickness was 100.10±5.70 µm in group A (low myopia), 86.80±5.20 µm in group B (moderate myopia) and 83.41±6.21 µm in group C (high myopia).

This finding is in agreement with **Mohamed** [9]**,** who reported significantly low RNFL thickness in participants with high (SE > -6) and moderate myopia (SE between -3.1 to - 5.99) compared with those with low myopia (SE > -3) in all quadrants except the temporal one (P=0.68)

Our results reported a significant positive correlation between spherical equivalent and RNFL thickness in the superior (r= 0.843, P < 0.001), inferior (r = 0.790, P < 0.001), nasal (r = 0.831, P < 0.001), temporal quadrants (r = 0.557, P < 0.001) and the average RNFL thickness (r = 0.722, P < 0.001). A strong correlation was noted in all quadrants except the temporal quadrant which showed weak correlation and this finding is consistent with finding that RNFL thickness in temporal quadrant is not affected by degree of myopia.

These findings were consistent with the results from previous studies. **Leung** ***et al.*** [10]**,** studied a total of 115 eyes of 115 healthy subjects, comprising 75 eyes with high myopia (SE > –6.0 D) and 40 eyes with low to moderate myopia (SE ranges from – 0.5 D to – 6.0 D). The mean age, axial length and SE were 35.9 ± 9.6 years (range: 22 to 60), 26.08 mm (range: 22.73 to 28.79) and -7.31 ± 3.04 D (range: –0.75 to –13.88) respectively. Total average and mean clock hour RNFL thicknesses were measured by OCT and compared between the two myopia groups. Apart from the temporal clock hours (8 – 11 o'clock), significant correlations were evident between RNFL measurements and SE. The average RNFL thickness decreased with decreasing SE (r = 0.291, P = 0.002).

Rauscher ***et al.*** [11], conducted a study on 27 subjects (10 female and 17 male). The mean age, axial length and SE were 34 ± 8 years (range: 23 to 54), 25.65 mm (range: 22.63 to 27.92), - 5.40 D (range: –1.25 to –11.25) respectively. A significant but less strong association was found between SE and RNFL thickness. RNFL thickness decreased with higher spherical equivalent (Overall R = −0.52, P=0.005, Superior R = −0.41, P=0.03, Inferior R = −0.45, P=0.02). Overall RNFL thickness decreased 3 microns for every 1 diopter sphere. Nasal and temporal RNFL thickness showed no significant associations with myopia**.**

Mohamed [9]**,** conducted a study on 98 eyes of 49 healthy subjects (33 female and 16 male). The mean age and SE were 26.52 ± 6.2 years (range: 21 to 45) and -5.33 ± 2.56 D (range: - 1.13 to -12.63) respectively. The participants were categorized into low myopia (SE > -3), moderate myopia (SE between -3.1 to -5.99), and high myopia (SE < -6). A significant linear correlation was noted between the SE and the RNFL thickness in the superior (r = 0.386, P = 0.0001) and inferior quadrants (r = 0.448, P = 0.0001), and the average RNFL thickness (r = 0.373, P = 0.0001). However, the nasal and temporal quadrants had no significant association with the SE.

In contrast, some other studies reported no correlation between high myopia and average RNFL thickness. **Hoh** ***et al.*** [3]**,** conducted a prospective observational case series study on 132 young males. All were male Asians (114 ethnic Chinese, 11 ethnic Malays, and 7 ethnic Indians). The mean age was 21.2 ± 1.1 years (range, 19 –24). The mean spherical equivalent (mean ± standard deviation) was –6.02± 3.46 D (range, 0.50 to 14.25), and the mean axial length was 26.0±1.42 mm (range, 23.22–29.23). The mean RNFL thickness measured by OCT was 101.1 ± 8.2 um [95% confidence interval, 99.4 – 102.8]. They reported no correlation between the mean peripapillary RNFL thickness and SE for the 3.40 mm (r = 0.11, P= 0.22), 4.50 mm (r = 0.103, P = 0.24) scan diameters.

Bowd ***et al.*** [5]**,** studied a group of 155 subjects with SE ranges from – 5.0 to + 5.0 D. They reported weak correlation between SE with any of RNFL parameters measured by HRT, GDx, and OCT**.**

As regard the axial length, our results reported a significant negative correlation between axial length and RNFL thickness in the superior (r= -0.831, P = 0.001), inferior (r = -0.720, P = 0.001), nasal (r = -0.830, P = 0.001), temporal quadrants (r = - 0.558, P = 0.001) and the average RNFL thickness (r = -0.711, P = 0.001). A strong correlation was noted in all quadrants except the temporal quadrant which showed weak correlation and this finding is consistent with finding that RNFL thickness in temporal quadrant is not affected by degree of myopia. These findings were consistent with the results from many previous studies which reported negative correlation between axial length and RNFL thickness. **Leung** ***et al.*** [10] reported a significant negative correlation between axial length and RNFL thickness in each clock hour except in the temporal sector (8 –11 o'clock). The average RNFL thickness decreased with increasing axial length (r = -0.314, P = 0.001).

Schweitzer ***et al.*** [13]**,** studied 10 patients (20 eyes) with high myopia and 10 control subjects (20 eyes) matched for age and sex. The mean RNFL thickness measured by OCT in the control and myopic groups was 108.8 ± 10.6 um and 80.0 ± 18.6 um respectively. A negative correlation (r= – 0.712, P < 0.001) was found between RNFL thickness and axial length.

In the study conducted by **Rauscher *et al.*** [11]**,** a significant, strong association was found between axial length and RNFL thickness. RNFL thickness decreased with higher axial length (Overall R = −0.70, P <0.001, Superior R = −0.60, P =0.001, Inferior R = −0.60, P=0.001). Overall RNFL thickness decreased 7 microns for every 1 mm of axial length. Nasal and temporal RNFL thickness showed no significant associations with myopia.

Budenz *et al.* [12]**,** conducted a study on three hundred twenty-eight normal subjects of whom 155 were men (48%) and 171 were women (52%). Mean age was 47.4 years (SD, 15.8; range, 18– 85). Mean axial length was 23.8 mm (SD, 1.1; range, 20.4–28.1). Spherical equivalent ranged from −11.75 to +6.75 diopters (D), with a mean refractive error of −0.54 (SD, 1.9). Retinal nerve fiber layer thickness was associated significantly with axial length—the longer the eye, the thinner is the mean RNFL (P<0.001).

For every 1-mm-greater axial length, RNFL thickness was thinner by approximately 2.2 μm (95% CI, 1.1–3.4) [12].

In contrast, **Hoh *et al.*** [3], reported no correlation between AL and RNFL thickness for the 3.40 mm (r = -0.04, P = 0.62) and for the 4.5 mm (r=0.03, P =0.75) scan diameters.

The difference between the results in current study and other studies which reported no correlation between myopia and RNFL thickness may be due to that the latter studies may have been limited by the poorer resolution of the earlier generation OCT and confocal laser devices and thus lower sensitivity.

As regard the age, it remains unclear whether the age could affect the RNFL thickness. In present study, no correlation was found between age and RNFL thickness in myopic subjects and this result might be due to that the age range was narrow and confined to three decades only.

Some studies have found significant correlations between age and the average RNFL thickness, but a lack of correlation between age and RNFL thickness in myopic participants was found in other studies.

Budenz *et al.* [12]**,** examined 328 normal participants with age ranging between 18 and 85 years, and found a small but significant correlation with age (2 mm of RNFL thinning/ decade). In another study, **Leung *et al.*** [10]**,** found no effect of age on RNFL thickness.

Regarding the sex, its effect on RNFL thickness was investigated in current study which showed no significant difference in RNFL thickness between men and women. This is consistent with results from other studies [5].

CONCLUSION

- High myopia should be considered in the interpretation of OCT data because of thinning of RNFL thickness and normative database corrected for refractive error and axial length should be incorporated.
- It is difficult for OCT to discriminate between high myopes with and without glaucoma. Therefore, clinical signs of glaucomatous nerve fiber damage are very important.
- Analysis of ganglion cell complex should be considered in patients with peripapillary atrophy.

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