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Effects of Refractive Status and Axial Length of the Eye on Retinal Nerve Fibre Layer Thickness Measured by OCT

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Abstract: *Background:* Retinal nerve fibre layer (RNFL) thickness is an important indicator in diagnosis and monitoring of optic disc diseases. RNFL thickness is affected by many factors such as race and age. Refractive errors are the most common ocular problem affecting all age groups, and affect ocular structures such as retina and optic nerve. Optical coherence tomography (OCT) is a non-invasive instrument that provides accurate measurements of RNFL thickness and detects early structural changes. This technique is safe, repeatable and quick. *Objective:* To evaluate the influence of refractive status and axial length of the eye on retinal nerve fibre layer (RNFL) thickness in emmetropics, myopics and hyperopics. *Materials and Methods:* It was a cross-sectional study, included 192 subjects (384 eyes) aged 18 to 30 years, who were divided into 3 main groups based on postcycloplegic spherical equivalent (SE), the subjects were also divided into groups based on their axial length (AXL). Retinal nerve fibre layer thickness was measured by OCT, axial length was measured by ultrasound A scan. *Results:* Thicknesses of Average RNFL, (Superior Temporal, Superior Nasal, Inferior Nasal, Nasal) sectors decreased with myopia and increased with hyperopia and this was statistically significant (p=0.0001), thicknesses also decreased with increasing of axial length and this was statistically significant (ST, SN, IN P-value =0.0001, N P-value =0.02, Avg. P-value =0.001). Thicknesses of (Temporal, Inferior Temporal) sectors decreased with hyperopia and increased with myopia and this was statistically significant (T P-value =0.0001, IT P-value=0.004), thicknesses also decreased with decreasing of axial length and this was statistically significant (T P-value=0.03, IT P-value= 0.001). *Conclusion:* Refractive status and axial length affect RNFL thickness, so they should be considered in mind before making any ocular diagnosis in which the RNFL is a diagnostic criteria.

Keywords: Spherical Equivalent (SE), Axial Length (AXL), Retinal Nerve Fibre Layer (RNFL), Optical Coherence Tomography (OCT)

1. Introduction

During optic nerve development, 2.85 million nerve fibers exist, but by the third trimester, we lose about 35% [1]. Knowing and understanding the determinants that affect the RNFL thickness help us in the diagnosis and monitoring of optic nerve diseases. Previous studies have found that white race [2], lower birth weight [3], longer axial length, and myopia have been associated with a thinner RNFL [4]. On the contrary, optic disc tilting [5], and Asian or Hispanic race have been associated with a thicker RNFL [2]. Retinal nerve fibre layer thickness is a sensitive and important indicator for predicting early glaucomatous changes, structural change is known to precede functional damages [6].

Refractive errors are the most common ocular problem affecting all age groups. Recent studies and World Health Organization (WHO) reports indicate that refractive errors are the first cause of visual impairment and the second cause of visual loss worldwide as 43% of visual impairments are attributed to refractive errors [7].

The E.P.P (Estimate pool prevalence) of myopia in adults was 26.5%, Myanmar had the highest prevalence (51.0%), and India had the lowest prevalence (4.4%), South-East Asia 32.9% and America 16.2% [8]. The E.P.P of hyperopia in adults was 30.6%, Africa had the highest prevalence 38.6%, followed by America 37.25% while Europe had the lowest prevalence 23.1% [8].

The prevalence of myopia is high in patients with ocular hypertension, primary open-angle glaucoma, and normal-tension glaucoma [9]. The risk of developing glaucoma is two to three times higher in myopic individuals than in nonmyopic individuals [9]. Myopics often have enlarged optic discs with a more oval configuration and larger areas of peripapillary atrophy [10], because of these features, glaucomatous changes can't be easily interpreted in myopic disc, possibly leading to a misdiagnosis of glaucoma.

The aim of this study is to evaluate the effect of refractive status and axial length of eyeball on retinal nerve fibre layer thickness.

2. Materials and Methods

2.1. Design Study

A cross sectional study.

2.2. Subject

Three main groups (hyperopics, myopics, and emmetropics) were recruited from the outpatient ophthalmic clinic of Tishreen University Hospital in Lattakia, Syria. From March 2019 till March 2020.

2.2.1. Ethical Considerations

An informed consent and ethical committee clearance were taken for this study.

2.2.2. Inclusion Criteria

Hyperopic and myopic patients, aged from 18 to 30 years/ both genders. Age and sex matched subjects who were emmetropics were recruited as controls.

2.2.3. Exclusion Criteria

Best corrected visual acuity (BCVA) worse than 20/20. Patients who have undergone surgery (cataract, vitrectomy, refractive surgery), glaucoma, amblyopia, retinal and optic nerve diseases, active corneal infection, corneal scars, blurred media, systemic diseases with ocular complications, previous trauma on the eye.

2.3. Procedures

Personal details of all participants such as (name, age, sex, phone number, and detailed clinical history) were written in a questionnaire.

All subjects underwent a comprehensive ophthalmological examination: Refraction before and after cycloplegia (1% cyclopentolate), visual acuity and best corrected visual acuity, intraocular pressure (IOP) measured by the Goldman applanation tonometer, anterior segment examination, pupil dilation and fundoscopy (slit lamp with +90D lens, indirect ophthalmoscopy), axial length was measured by Aviso ultrasound A scan, retinal nerve fibre layer thickness was measured by a SD-OCT (Spectralis, Heidelberg Engineering). All RNFL thickness measurements were performed after cycloplegia, by a single experienced operator, scans were centered on the optic disc with a scanning diameter of 3.5 mm. The Spectralis OCT software allowed for automatic segmentation of the upper and lower borders of the RNFL to calculate the overall global average RNFL thickness (G). Peripapillary RNFL thickness values were divided into four quadrants. The superior and inferior quadrants were further divided into nasal (N) and temporal (T) sectors. All RNFL region subfields included superior temporal (ST), temporal (T), inferior temporal (IT), superior nasal (SN), nasal (N), inferior nasal (IN). The RNFL thickness of the 6 subfields and the global RNFL thickness were recorded in micrometers.

2.4. Statistical Analysis

Descriptive statistical: the quantitative data (arithmetic mean, standard deviation), and the qualitative ones (frequencies and percentile values). Inferential statistical: one-way analysis of variances (ANOVA), correlation analyses were performed using Pearson's correlation coefficient for parametric data. The data were analyzed by SPSS (Statistical Package for the Social Sciences) version 19. The statistical analysis was done at significance level of 5%.

3. Results

A total of 192 participants (384 eyes) were enrolled in this study, 64 males (33.30%), 128 females (66.70%). Participants were divided into 3 main groups due to their spherical equivalent after cycloplegia. 1. emmetropics (80 individuals, 160 eyes), 2. myopics (74 patients, 148 eyes), 3. hyperopics (38 patients, 76 eyes). Myopics and hyperopics were divided into subgroups, low myopia SE [-0.50, -3.00], moderate myopia SE [-3.25, -6.00], high myopia SE > -6.00, low hyperopia SE [+0.50, +2.00], moderate hyperopia SE [+2.25, +5.00], high hyperopia SE >+5.00. We haven't recruited high hyperopia patients meeting inclusion criteria during the study period.

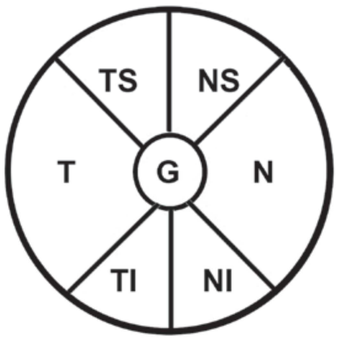

Figure 1. *Depiction of the six standard subfields and the average of the retinal nerve disc*

Table 1. *Demographic profile of the subjects in the study groups.*

	Emmetropics	Myopics			Hyperopics		
		Low myopia	Moderate myopia	High myopia	Low hyperopia	Modeate hyperopia	P-value
Sex female/male	52/28	21/13	23/4	8/5	16/11	8/3	0.3
Age	26.1±2.6	25.08±3.3	25.6±2.9	25.5±3.6	25.4±2.8	24.7±3.2	0.4
arithmetic mean of spherical equivalent after cycloplegia	0.02±0.1	-1.2±0.4	-4.04±0.6	-6.7±0.7	1.5±0.4	3.2±0.5	0.0001
Axial length (mm)	23.1±0.2	24.1±0.1	24.8±0.2	25.2±0.2	22.9±0.1	22.7±0.1	0.0001

Table 2. *Comparison of RNFL thickness in the different SE groups according to Avg. RNFL thickness.*

Study groups	N (number of eyes in each group)	Average RNFL thickness (Mean ± SD)	p-value
Emmetropia	160	107.9±3.7	0.0001
Low myopia	68	103.8±2.2	
Moderate myopia	54	99.7±3.9	
High myopia	26	90.8±5.3	
Low hyperopia	54	113.07±1.8	
Moderate hyperopia	22	114.9±1.5	

Table 3. *Analysis of variance of RNFL thickness in the different SE groups according to RNFL subfields.*

Study groups	ST	T	IT	SN	N	IN
Emmetropia	144.2±6.8	74.07±8.4	146.6±6.9	111.6±6.1	79.2± 3.8	108.7± 5.08
Low myopia	142.1±4.8	75.5±9.8	150.7±3.07	110.9±0.9	78.02±5.7	103.6±3.4
Moderate myopia	141.9±5.5	76.6±6.4	153.8±6.8	107.6±6.4	77.03±8.4	97.3±6.2
High myopia	128.8±5.4	77.5±6.7	154.1±1.3	90.6±4.8	75.6±7.6	75.3±4.2
Low hyperopia	146.1±1.3	72.4±2.8	144.8±3.8	122.7±2.5	82.8±2.1	148.2±1.9
Moderate hyperopia	148.2±1.3	70.1±5.2	142.8±2.6	124.6±2.4	84.03±2.2	148.8±1.2
P-value	0.0001	0.004	0.0001	0.0001	0.0001	0.0001

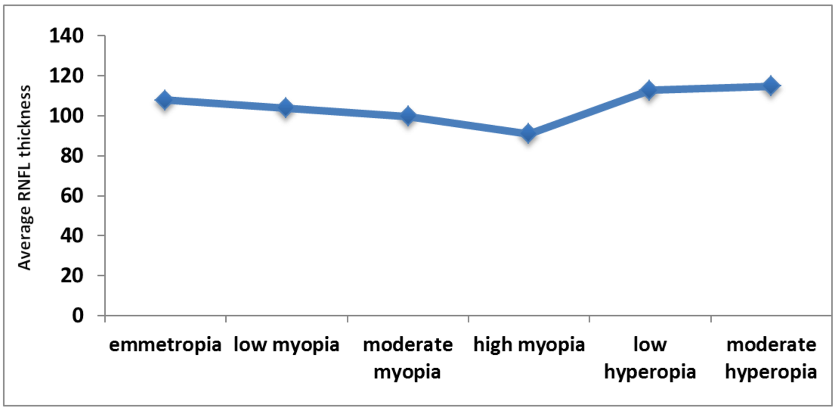

Figure 2. *Mean Avg. RNFL thickness in the study groups.*

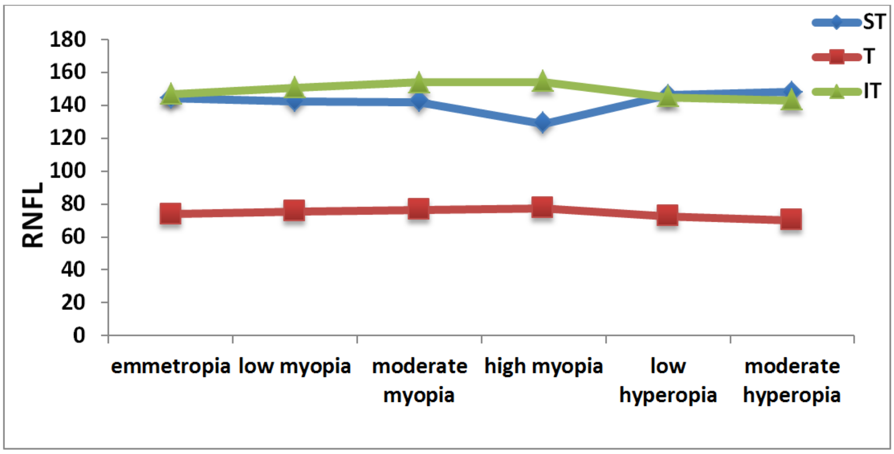

Figure 3. *Mean RNFL thickness in the temporal sectors.*

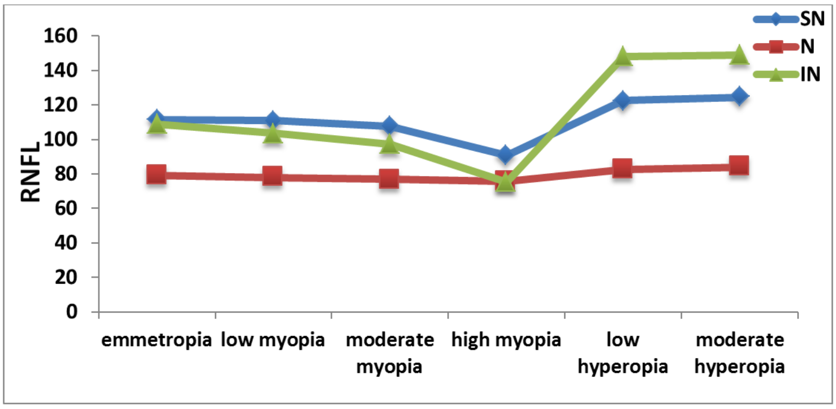

Figure 4. *Mean RNFL thickness in the nasal sectors.*

We have found in table 2 that Avg. RNFL thickness was thinner in myopics compared to emmetropics, and the thickness became less with increasing of myopia. Avg. RNFL thickness was thicker in hyperopics compared to emmetropics, and the thickness increased with increasing of hyperopia. And that was statistically significant, P-value=0.0001.

We have observed in table 3 that the thicknesses in the subfields (ST, SN, N, IN) were thinner in myopics compared to controls, and with increasing of myopia the thicknesses became less. While the thicknesses in (ST, SN, N, IN) were thicker in hyperopics compared to controls, and with increasing of hyperopia the thicknesses increased too. And that was statistically significant (P-value =0.0001). The thicknesses in the subfields (T, IT) were thicker in myopics compared to controls, and with increasing of myopia the thicknesses increased too.

Table 4. *Correlations of RFNL (Global and subfields) thicknesses with Spherical equivalent.*

	R	P-value
ST	0.5	0.0001
T	-0.2	0.03
IT	-0.5	0.0001
SN	0.7	0.0001
N	0.3	0.002
IN	0.8	0.0001
Avg. RNFL	0.8	0.0001

While (T, IT) thicknesses were thinner in hyperopics compared to controls, and became less with increasing of hyperopia. And that was statistically significant (T. P= 0.004, IT. P=0.0001).

We have studied the relation between RNFL thickness and spherical equivalent using Pearson's correlation coefficient. We have found in table 4 that thicknesses in (ST, SN, N, IN) sectors and Avg. RNFL thickness had a positive correlation with SE (ST r= 0.5, SN r=0.7, N r=0.3, IN r=0.8, Avg. r =0.8). Thicknesses in (T, IT) sectors had a negative correlation with SE (T r= -0.2, IT r= -0.5).

We divided all participants into 3 groups according to their AXL, 1. AXL [21-22.99 mm], 2. AXL [23-24.99 mm], 3. AXl > 25mm. We recorded the thicknesses in the 6 subfields and Avg. RNFL thickness.

In table 5, there was a statistically significant differences in RNFL thickness between the 3 groups according to AXL.

We have studied the relation between AXL and RNFL thickness using Pearson's correlation coefficient. In table 6 we have found that thicknesses in (ST, SN, N, IN) sectors and Avg. RNFL thickness had a negative correlation with AXL (ST r= - 0.3, SN r= - 0.6, N r= - 0.1, IN r= - 0.7, Avg. r= - 0.8). Thicknesses in (T, IT) sectors had a positive correlation with AXL (T r=0.1, IT r= 0.3).

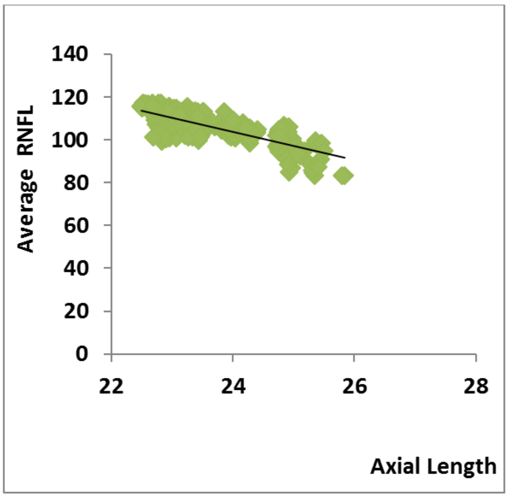

Figure 5. *Correlation between Avg. RNFL thickness and AXL.*

Table 5. *Analysis of variance of RNFL thickness in the different AXL groups according to RNFL subfields and Avg. RNFL.*

Axial length	Avg. RNFL	ST	T	IT	SN	N	IN
21 – 22.99 (mm)	111.04±4.06	146.2±5.01	73.5±6.9	145.7±5.6	117.3±7.8	80.7±4.1	127.09±19.9
23 – 24.99 (mm)	104.8±5.4	142.6±6.1	74.7±8.2	149.2±6.7	110.9±6.8	78.7±6.2	107.4±14.6
25< (mm)	91.4±5.5	129.3±5.6	77.7±6.9	154.1±1.4	91.5±4.7	76.8± 2.4	75.7±4.3
P-value	0.001	0.0001	0.03	0.001	0.0001	0.02	0.0001

Table 6. *Correlation of RNFL (Global and subfields) thickness with Spherical Equivalent.*

	R	p-value
ST	-0.3	0.001
T	0.1	0.03
IT	0.3	0.02
SN	-0.6	0.0001
N	-0.1	0.04
IN	-0.7	0.0001
Avg. RNFL	-0.8	0.0001

4. Discussion

We have found in our study that Avg. RNFL thickness in emmetropics was 107.9±3.7μm, Avg. RNFL thickness values in low, moderate and high myopic groups were (103.8±2.2, 99.7±3.9, 90.8±5.3) μm respectively, and P-value= 0.0001. Avg. RNFL thickness values in low, moderate hyperopic groups were (113.07±1.8, 114.9±1.5) μm respectively, P-value=0.0001. Avg. RNFL is thicker in hyperopics then in emmetropics and then in myopics. This is similar to results of previous studies.

A study had been prepared by Nigwekar et al [11], included 70 participants aged 20 to 40 years, found that Avg. RNFL in emmetropics was 94.87±7.24μm, Avg. RNFL thickness values in low, moderate, and high myopic groups were (90.68±8.74, 84.60±9.46, 81.14±6.07) μm respectively. Avg. RNFL thickness values in low, moderate hyperopic groups were (96.5±3.02, 99.68±2.39) μm respectively.

Another study had been prepared by Yi Zha et al [12], included 271 participants (myopics and controls), found that Avg. RNFL thickness in emmetropics was 104.76±10.15μm. Avg. RNFL thickness values in low, moderate and high myopic groups were (101.46±7.95, 99.15±8.94, 90.57±10.07) μm respectively.

V. sowmya et al [13], found in their study that included 150 participants. Avg. RNFL thickness in emmetropics was 111.75±4.83μm, Avg. RNFL thickness values in low, moderate myopic groups were (111.15±5.1, 105.05±6.82) μm respectively. Avg. RNFL thickness values in low and moderate hyperopic groups were (113.47±5.51, 114.68±5.1) μm respectively.

Differences in the values may be due to different race or different devices of OCT.

We have found that (ST, SN, N, IN) thicknesses were thinner in myopics than emmetropics, while they were thicker in hyperopics than emmetropics P=0.0001. (T, IT) thicknesses were thicker in myopics than emmetropics, and they were thinner in hyperopics than emmetropics (T P=0.0001. IT P=0.004).

A study had been prepared by Veysi et al [14], included 98 participants, found that thicknesses in all subfields were thinner in myopics than emmetropics, and thicker in hyperopics than emmetropics. And that was statistically significant in all subfields except the nasal sector P=0.13. Another study had been prepared by Kausar et al [15], included 93 participants, found that (IN, IT, N, SN) thicknesses were thinner in myopics than emmetropics, and that was statistically significant only in IN sector P=0.001. Thicknesses in (ST, T) were not affected by refractive status (thicker in emmetropics, then hyperopics, then myopics).

Yi Zha et al [12] found that (ST, SN, N, IN, IT) thicknesses decreased with myopia, while (T) thickness increased with myopia.

We have found that (Avg. RNFL, ST, SN, N, IN) thicknesses decreased with increasing of AXL, and that was statistically significant, (T, IT) thicknesses increased with the increasing of AXL, and that was statistically significant. A previous study had been prepared by Abinhav et al [16], included 149 participants, found that Avg. RNFL thickness and thicknesses in all subfields decreased with increasing of AXL, and that was statistically significant except (T, N) sectors, P= 0.13, 0.38 respectively. This study differed with us in age (10-70 years), race, and using another OCT device (RTVue three-dimensional Fourier domai).

5. Conclusion

Refractive status and axial length affect retinal nerve fibre layer thickness.

There is a positive correlation between SE and (Avg. RNFL, ST, SN, N, IN) thicknesses, while the correlation between SE and (T, IT) thicknesses is negative.

There is a negative correlation between AXL and (Avg. RNFL, ST, SN, N, IN) thicknesses, while the correlation between AXL and (T, IT) thicknesses is positive.

Our study suggests that the diagnosis of ocular diseases may be improved by considering refractive status and axial length while measuring RNFL thickness.

Conflicts of Interest

All the authors do not have any possible conflicts of interest.

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