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ORIGINAL STUDY

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The Peripapillary Retinal Nerve Fiber layer thickness in Subjects with Emmetropia, Mild Myopia, and Mild Hypermetropia in an Iraqi Sample

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Abstract

Background: The measurement of retinal nerve fiber layer (RNFL) these days is possible with the high resolution optical coherence tomography (OCT).

Objectives: To measure the peripapillary retinal nerve fiber layer thickness in subjects with emmetropia, mild myopia and mild hypermetropia by using OCT.

Materials and methods: This is cross sectional descriptive study with a total of 182 healthy subjects who had visited Ibn Al Haitham eye teaching hospital the ages of the participants were between 18 to 40 years. The participants were randomly selected and categorized to three groups (emmetropic, mild myopic hypermetropia) each group was studied for the effect of age, axial length, spherical equivalent on RNFL thickness and the data were analyst using Pearson coefficient and multivariate linear regression models. The RNFL thickness was measured and compared in these three groups by using OCT.

Results: The correlation of spherical equivalent with average RNFL and the four quadrants thickness was insignificant. The axial length showed a weak negative correlation in the three study groups but that was statistically not significant. The right eyes on compared to the left showed significantly thicker nasal and temporal quadrants.

Conclusion: Mild myopia and hyperopia do not affect the peripapillary RNFL thickness significantly, on increasing the spherical equivalent there is increasing in RNFL thickness but this was statistically insignificant, on increasing axial length there is reduction in RNFL thickness and this was insignificant.

Keywords: Retinal nerve fiber layer, Myopia, Hypermetropia, Emmetropia

1. Introduction

The nerve fiber layer contains the axons of the ganglion cells (the so-called 'centripetal' or 'afferent' fiber), glial cells, a rich capillary bed and centrifugal (or efferent) fibers. The axons are arranged in arcades delineated by the processes of Muller and other glial cells [1].

During optic nerve development, 2.85 million nerve fibers exist, but by the third trimester, we lose about 35% [2]. The retinal nerve fiber layer is a most sensitive indicator of optic nerve damage in glaucoma as it precedes visual field loss [3, 4]. Age [5], gender, axial length, size of the optic disc, refractive status of the eye [6, 7]. Ethnicity and race [8], can affect the RNFL thickness. The relationship of the RNFL thickness with axial length and refractive error is very important and need to be considered when we evaluate RNFL thickness for disease status [9].

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In eye that has no refractive error when viewing distant objects is said to have emmetropia or be emmetropic [10]. Near-sightedness happen when the image is focused in front of the retina while far sightedness happen when the image is focused behind it [11].

Peripapillary RNFL thickness measurement by tomography (OCT) has been shown to be valuable in the diagnosis and monitoring of retinal diseases and glaucoma [12].

Optical coherence tomography (OCT) is a new diagnostic computerized technique, which is used for generating in vivo images of retinal nerve fiber layer (RNFL) thickness which is reproducible, quantitative, and objective it enables objective measurement of the optic nerve head, RNFL and macular thickness parameters [13].

OCT works on the principle of low-coherence interferometry, which generates retinal tomographs with a high-resolution cross-sectional image of the posterior pole of the eye, and can be useful in glaucoma diagnosis for its ability to study the diffuse and localized thinning of RNFL [14–16], Its ease of access to different areas in the eye allows its use as an excellent diagnostic technology [17].

Spectral-domain optical coherence tomography (SDOCT) is superior to time-domain OCT in performing scanning with higher axial resolution, better reproducibility [18]. Earlier defect in the retinal nerve fiber layer (RNFL) measured by OCT provide an excellent objective and quantitative method in the diagnosis and management of glaucoma [19–21].

The aim of this study is to measure the peripapillary RNFL thickness in subjects with emmetropia and those with mild myopia and mild hypermetropia.

2. Materials and methods

This is a cross-sectional descriptive study in which a total number of 182 participants of the subjects who visited Ibn Al-Haitham teaching eye hospital in Baghdad during time period between August 2018 to September 2019 were included. A verbal consent was taken from all the patients to participate in the study.

From those 182 subjects (364 eyes), fifty-two (104 eyes) participants were having mild myopia with spherical equivalent less than −3 diopter, and one hundred participants (200 eyes) were emmetropic with no refractive error and nil correction, and thirty participants (60 eyes) with mild hyperopia with spherical equivalent less than +2 diopter. Both right and left eyes were incorporated in the current study.

2.1. *Inclusion criteria*

Subjects age range from 18 to 40 years old who had either, mild myopia, mild hypermetropia or emmetropia with no ocular or systemic diseases that affect retina or the RNFL thickness.

2.2. *The exclusion criteria*

1. Astigmatism more than 1 diopter.
2. Best corrected visual acuity less than 20/20.
3. Amblyopia.
4. Retinal and optic disc disease.
5. Corneal disorders, cataract, strabismus, glaucoma, ocular hypertension.
6. Intraocular and refractive surgeries or ocular trauma.
7. Neurological diseases or diabetes.

The subjects where from both gender male and female for each participant a detailed history was taken and complete examination of both eyes, including visual acuity, auto refraction, applanation tonometry, slit lamp examination of anterior and posterior segment examination by +90D and +78D lens was done. In each group the age, gender, axial length, spherical equivalent, average RNFL along with superior, inferior, temporal and nasal quadrants thickness data were studied.

The influence of the spherical equivalent, axial length and age on average and the four quadrants of RNFL thickness was studied.

In each group both eyes were studied separately and then combined for the axial length and for average and quadrants RNFL thickness.

The axial length was examined by millimeter and the examination was done by using IOL master 500 type Carl Ze iss advanced technology v.7.5.

The OCT examination was performed by a trained technician using Carl Zeiss Meditec (Cirrus HD OCT 5000), Inc. device with peripapillary diameter of 3.4 mm with signal strength more than 6 was taken as acceptable and thickness was measured by micrometer.

3. Statistical analysis

Data tabulation, input and coding were done by the use of IBM©SPSS©(Statistical Package for the Social Sciences) Statistics Version 23. Univariate ANOVA for comparison between more than two numerical variables, as the data was normally distributed. Pearson correlation models were conducted to assess

Table 1. Demographic data of the study groups.

Variable	Emmetropia Mean ± SD	Myopia Mean ± SD	Hypermetropia Mean ± SD	p-value
Age in year	32.28 ± 6.8$^{>M}$	25.79 ± 7.5$^{<E\&H}$	30 ± 9.4$^{<E}$	<0.001*
Gender	No.(%)	No.(%)	No.(%)	
Male	47(63.5)	14(18.9)	13(17.6)	0.054**
female	53(49.1)	38(35.2)	17(15.7)	
Total no.	100	52	30	182

*: One-way ANOVA with Tukey's post hoc test, **: Chi-square test H: hypermetropic, M: myopic, E: emmetropic.

Table 2. Both eyes AL and RNFL thickness according to study groups.

Variable	Emmetropia Mean ± SD	Myopia Mean ± SD	Hypermetropia Mean ± SD	p-value
AL	23.65 ± 0.7$^{>H}$	24 ± 0.8$^{>H}$	22.8 ± 1$^{<E\&M}$	<0.001
Av-RNFL	92.95 ± 7.2	90.81 ± 10.4	93.47 ± 8.7	0.273
Sup-RNFL	116.01 ± 10.9	114.65 ± 19	115.55 ± 17.8	0.874
Inf-RNFL	120.57 ± 15.9	117.76 ± 16.4	122.77 ± 14.1	0.359
Temp-RNFL	63.39 ± 7	61.39 ± 9.4	62.35 ± 7.2	0.338
Nas-RNFL	70.79 ± 10.5	69.35 ± 10.2	72.65 ± 8.8	0.396

*: One-way ANOVA with Tukey's post hoc test, AL: axial length, Av: average, Sup: superior, Inf: inferior, Temp: temporal, Nas: nasal H: hypermetropic, M: myopic, E: emmetropic.

the correlation the variables, and multivariate linear regression model was used to predict the changes in retinal nerve fiber layer thickness attributed to spherical equivalent and axial length. *P-value* less than 0.05 was considered significant throughout data analysis.

4. Results

There were statistically significant differences between study groups regarding age, as myopes were younger than emmetropes and hyperopes, and the latter were younger than the former, as shown in (Table 1).

In both eyes, the AL was significantly lower in hyperopes compared to both myopes and emmetropes, while RNFL thickness had no statistically significant differences across the study groups, as shown in Table 2.

In both myopic and hyperopic subjects the RNFL thickness increased with increasing SE (thicker in less myopic in myopic individuals and more hyperopic in hypermetropia group), although these correlations were weak with no statistical significance.

The multivariate linear logistic regression model predicted the change in RNFL thickness with increasing the SE by one diopter (in myopic patients the increment in SE meant more myopia by −1 diopter), and it revealed that with each diopter myopic shift there was a −0.125 μm reduction in average RNFL, as shown in (Table 4).

The change in RNFL thickness in hyperopic individuals was regarded per +1 diopter increment in SE, and the average RNFL thickness was associated with +0.052 increment with each diopter of hyperopic shift, as shown in (Table 5).

In the three refractive groups, the axial length has a negative correlation with average retinal nerve fiber layer thickness, but this was statistically insignificant. The four quadrants thickness correlation with the axial length showed that:

Table 3. Correlation between SE and RNFL thickness according to refractive errors.

Variable	Myopia	Hyperopia
Av-RNFL	0.150	0.315
Sup-RNFL	0.090	0.311
Temp-RNFL	0.143	0.006
Nas-RNFL	0.091	0.130

Pearson correlation coefficient *: significant (P-value < 0.05) **: highly significant (P-value < 0.01) SE: spherical equivalent RNFL: retinal nerve fiber layer.

Table 4. Linear regression model of both eyes SE and RNFL thickness according to myopic eyes.

Quadrant	β	SE	p-value*
Av-RNFL	−0.125	0.077	0.112
Sup-RNFL	−0.03	0.021	0.159
Inf-RNFL	−0.027	0.018	0.136
Temp-RNFL	−.021	0.024	0.381
Nas-RNFL	−0.029	0.025	0.249

*: Multivariate linear regression model, Av: average, Sup: superior, Inf: inferior, Temp: temporal, Nas: nasal, SE: Standard error, β:correlation coefficient.

Table 5. Linear regression model of both eyes absolute SE and RNFL thickness according to hyperopic eyes.

Quadrant	β	SE	p-value*
Av-RNFL	0.052	0.235	0.828
Sup-RNFL	0.003	0.06	0.954
Inf-RNFL	0.003	0.06	0.967
Temp-RNFL	0.023	0.057	0.686
Nas-RNFL	0.019	0.063	0.771

*: Multivariate linear regression model, Av: average, Sup: superior, Inf: inferior, Temp: temporal, Nas: nasal, SE: Standard error, β:correlation coefficient.

Table 6. Correlation between, AL and RNFL thickness according to refractive errors.

Quadrant	Myopia	Hyperopia	Emmetropia
Av-RNFL	−0.042	−0.191	−0.065
Sup-RNFL	0.056	−0.08	−.031
Inf-RNFL	0.020	−0.304*	−0.05
Temp-RNFL	0.128	−0.316*	0.097
Nas-RNFL	−.259**	0.144	−0.105

Pearson correlation coefficient *: significant (P-value < 0.05) **: highly significant (P-value < 0.01).

Table 7. Linear regression model of both eyes AL and RNFL thickness according to hyperopic eyes.

Quadrant	β	SE	p-value*
Av-RNFL	−0.121	0.379	0.753
Sup-RNFL	−0.039	0.097	0.692
Inf-RNFL	−0.049*	0.096	0.04*
Temp-RNFL	−.070*	0.092	0.03*
Nas-RNFL	0.013	0.102	0.903

*: Multivariate linear regression model, Av: average, Sup: superior, Inf: inferior, Temp: temporal, Nas: nasal, SE: Standard error, β:correlation coefficient.

- In myopic group there is a negative correlation with the nasal quadrants which is significantly high.
- In hypermetropic group there is statistically significant negative correlation between axial length and the inferior and temporal quadrants.
- In emmetropic group there is no statistically significant correlation between axial length and the four quadrants thickness. Those findings are shown in (Table 6).

The average nerve fiber layer decreased −0.121 μm with each increase in one mm of AL in hyperopic, and −0.147 μm in myopic, while −0.054 μm in emmetropic eyes.

The correlation between age and average RNFL thickness in the three study groups showed that:

- There is a significant negative correlation in the emmetropic group.
- In hyperopic group there is a weak negative correlation that is not statistically significant.

Table 8. Linear regression model of both eyes AL and RNFL thickness according to myopic eye.

Quadrant	β	SE	p-value*
Av-RNFL	−0.147	0.073	0.09
Sup-RNFL	0.047	0.02	0.067
Inf-RNFL	0.031	.017	.073
Temp-RNFL	0.052	0.023	0.084
Nas-RNFL	−0.067**	0.024	0.001**

*: Multivariate linear regression model, Av: average, Sup: superior, Inf: inferior, Temp: temporal, Nas: nasal, SE: Standard error, β:correlation coefficient.

Table 9. Linear regression model of both eyes AL and RNFL thickness according to emmetropic eyes.

Quadrant	β	SE	p-value*
Av-RNFL	−0.054	0.061	0.373
Sup-RNFL	−0.017	0.018	0.351
Inf-RNFL	−0.011	0.013	0.425
Temp-RNFL	.023	0.02	0.250
Nas-RNFL	−0.007	0.018	0.340

*: Multivariate linear regression model, Av: average, Sup: superior, Inf: inferior, Temp: temporal, Nas: nasal, SE: Standard error, β:correlation coefficient.

Table 10. Correlation between age and RNFL thickness according to refractive errors.

Quadrant	Myopia	Hyperopia	Emmetropia
Av-RNFL	−0.056	−0.097	−0.163*
Sup-RNFL	−0.055	−.146	−.013
Inf-RNFL	0.164	.174	−.055
Temp-RNFL	0.100	.184	−.102
Nas-RNFL	0.16	−.45**	−0.278**

Pearson correlation coefficient *: significant (P-value < 0.05) **: highly significant (P-value < 0.01).

- In myopic group, the correlation was insignificant.

While the correlation between the age and the quadrants thickness in the four groups showed that:

- In emmetropic and hyperopic groups there was no significant correlation in the superior, inferior, temporal quadrants, while the nasal quadrant showed a negative correlation which is significantly high.
- In myopic group there is no significant correlation between age and quadrants thickness. Those findings are shown in (Table 10).

On examining the left eye alone the hyperopes had statistically significant lower AL compared to the other two groups, while RNFL thickness in the different quadrants had no statistically significant differences across the study groups, as shown in (Table 11).

Table 11. The mean of the Left eyes AL and RNFL thickness according to study groups.

Variable	Emmetropia Mean ± SD	Myopia Mean ± SD	Hypermetropia Mean ± SD	p-value
AL	$23.67 \pm 0.7^{>H}$	$24 \pm 0.8^{>H}$	$22.8 \pm 1^{<E\&M}$	<0.001
Av-RNFL	93.38 ± 7.2	91.1 ± 10.4	93.7 ± 8.7	0.290
Sup-RNFL	114.01 ± 10.9	112.65 ± 19	115.07 ± 17.8	0.820
Inf-RNFL	121.57 ± 15.9	117.76 ± 16.4	123.77 ± 14.1	0.193
Temp-RNFL	64.39 ± 7	61.39 ± 9.4	62.35 ± 7.2	0.325
Nas-RNFL	72.29 ± 10.5	69.35 ± 10.2	72.65 ± 8.8	0.662

*: One-way ANOVA with Tukey's post hoc test, AL: axial length, Av: average, Sup: superior, Inf: inferior, Temp: temporal, Nas: nasal H: hypermetropic, M: myopic, E: emmetropic.

Table 12. The mean of the Right eyes AL and RNFL thickness according to study groups.

Variable	Emmetropia Mean ± SD	Myopia Mean ± SD	Hypermetropia Mean ± SD	p-value
AL	$23.65 \pm 0.7^{>H}$	$24 \pm 0.8^{>H}$	$22.8 \pm 1^{<E\&M}$	<0.001
Av-RNFL	92.95 ± 7.2	90.81 ± 10.4	93.47 ± 8.7	0.396
Sup-RNFL	116.01 ± 10.9	116.65 ± 19	116.55 ± 17.8	0.985
Inf-RNFL	118.57 ± 15.9	118.76 ± 16.4	122.77 ± 14.1	0.605
Temp-RNFL	62.39 ± 7	61.39 ± 9.4	62.35 ± 7.2	0.271
Nas-RNFL	69.79 ± 10.5	68.35 ± 10.2	72.65 ± 8.8	0.201

*: One-way ANOVA with Tukey's post hoc test, AL: axial length, Av: average, Sup: superior, Inf: inferior, Temp: temporal, Nas: nasal H: hypermetropic, M: myopic, E: emmetropic.

Table 13. Difference between of AL, and RNFL thickness according to laterality.

Variable	Right eye Mean ± SD	Left eye Mean ± SD	p-value
AL	23.65 ± 0.9	23.65 ± 0.9	0.984
Av-RNFL	92.95 ± 7.2	91.81 ± 10.4	0.359
Sup-RNFL	114.01 ± 10.9	116.65 ± 19	0.186
Inf-RNFL	120.57 ± 15.9	119.76 ± 16.4	0.344
Temp-RNFL	63.39 ± 7	61.39 ± 9.4	0.031
Nas-RNFL	71.82 ± 10.5	69.35 ± 10.2	0.034

Independent sample t-test AL: axial length, Av: average, Sup: superior, Inf: inferior, Temp: temporal, Nas: nasal.

In right eyes also AL was also significantly lower in hyperopes compared to both myopes and emmetropes, while RNFL thickness had no statistically significant differences across the study groups, as shown in (Table 12).

There were no statistically significant differences between laterality and AL, average, superior and inferior RNFL thicknesses, but in right eyes the temporal and nasal RNFLs were significantly thicker in comparison to left eyes, as shown in (Table 13).

The RNFL thickness followed the "ISNT" rule in all of the study groups, with statistically significant difference ($p < 0.001$) between quadratic thicknesses as shown in Fig. 1.

5. Discussion

Many investigative modalities have been utilized for the detection of retinal and optic nerve disease, the emergence of techniques such as OCT which use the combination of infrared light and computer analysis for more precise calculation and documentation of findings which have a valuable rule for this purpose [22].

In the current study, it was found that myopic subjects were younger than hypermetropic and emmetropic subjects, and this disparity in age was similarly reported in another study [23], which can be attributed to the environmental factors such as reading [24]. However, hypermetropic subjects were found to be even younger than emmetropic may be due to the balance between the crystalline lens development and the axial length development which tend to stabilize later on [25].

The p value for the gender difference between the three groups was 0.054 which was insignificant considering that in this study, the P value less than 0.05 was considered significant, this insignificant association was also found in the study conducted by Ayisha Kausar et al. [26].

To avoid statistical error of independent sampling each participant's eye was examined separately and then combined (Tables 2, 11 and 12), regarding the axial length and the average peripapillary RNFL and the four quadrants (superior, inferior, temporal, nasal) thickness.

- In either case there was a statistically significant difference in axial length with hypermetropic group having the lowest axial length in comparison to other groups and this was similar to the

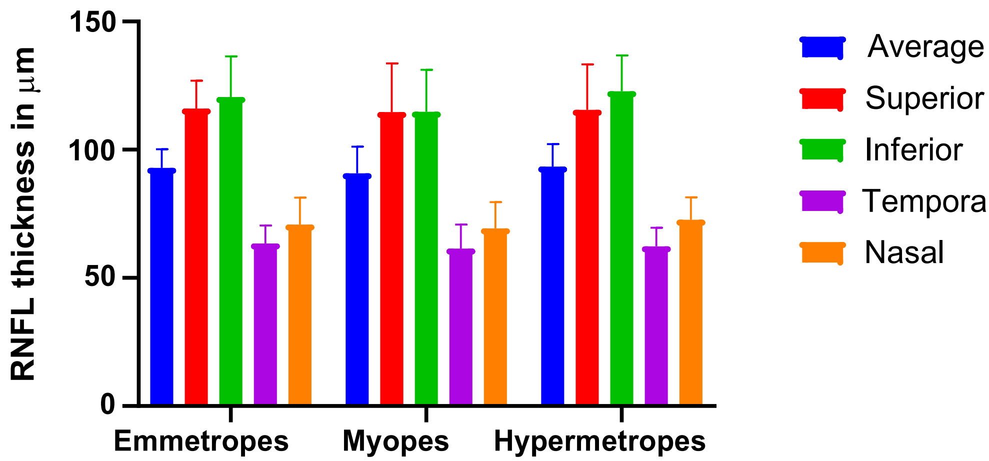

Fig. 1. Distribution of quadrants RNFL thickness according to study groups.

result of a study done by Lourdes lloerent et al. [27].

- While comparing the results in our study to the findings in a study done by Sowmya V et al. [21], it was found that in our study the average RNFL thickness for both eyes is 92.95 ± 7.2 μm in emmetropic group, 90.81 ± 10.4 μm in myopic group, and 93.47 ± 8.7 μm in hypermetropic group, which was less than the RNFL thickness found in the latter study. Also it was found that in each group of the present study the four quadrants RNFL thickness had a lower value than that in the abovementioned study and this may be due to the difference in each of sample size, population characteristics, and the difference in OCT device between the two studies.
- Also in the current study it was noted that there was a difference in the results regarding the average RNFL thickness with the hypermetropia having the highest value and the myopia having the lowest value although this difference was statistically insignificant and these findings were also found by Sowmya V et al. [21], which showed that only with refractive error more than 3 diopter there will be significant difference in average RNFL thickness. This may explain the results of the current study in which only mild myopia and hypermetropia were included.

Although the current study showed that there was an insignificant correlation between the spherical equivalent and the average and quadrants RNFL thickness, it appeared that there was an increase in thickness with hyperopic shift (the average RNFL thickness showed an increase of 0.052 μm for each one diopter increase in refractive error) and a decrease in thickness with myopic shift(for each one diopter myopic shift there is a reduction in average RNFL thickness equal to 0.125 μm) these findings were in agreement with results of Sowmya V et al. [21].

This study also found that the axial length had a weak negative correlation with average RNFL (for every 1 mm increase in axial length there will be an associated decrease in the average RNFL thickness which was equal to 0.121 μm in hyperopic, 0.147 μm in myopic,0.054 in emmetropic) but this was insignificant. No explanation for this insignificance was found because no studies was done to find the correlation between axial length and average RNFL thickness in mild refractive error. However one study with higher degrees of refractive error and wider range of axial length showed a significant negative correlation between axial length and peripapillary RNFL [28].

The correlation between the axial length and the RNFL quadrants thickness was also incorporated in this study and the result was variable, in emmetropia there was a weak negative correlation that is insignificant and this was in agreement with the finding in Fahmy RM et al. [9]. In mild myopia there is a significant negative correlation between axial length and nasal RNFL thickness and this was similarly reported in a study done by Chau-Yin Chen et al. [29]. In mild hypermetropia there was a significant decrease in the inferior and temporal quadrants that cannot be compared to publish data because no study was done to find the correlation between the axial length and mild hypermetropia RNFL quadrants thickness.

Many studies showed that with increasing age there will be a decrease in average RNFL thickness [30, 31]. This may explain the current study results that showed that in emmetropic subjects who had the oldest age between the three groups (mean age 32.28 ± 6.8 years) have a significant negative correlation, while the hypermetropic group being the second older age group in the study (mean age 30 ± 9.4 years) and myopic group (the youngest age group with mean age 25.79 ± 7.5 years) had no significant correlation between age and RNFL thickness. The RNFL quadrants thickness correlation with age in the current study showed that the nasal quadrants display highly significant thinning in emmetropic and hyperopic groups but not myopic group, and this contradict the results of study that was done in Taiwan in 2018 which showed that with increasing age there will be superior quadrant thinning [32] and this variability in the results may be due to racial difference along with sample size and age range difference since the latter study had larger number of participants with older age range.

On comparing right and left eyes there were no significant difference between laterality and axial length. A finding that is similar to other study results [33, 34]. While in applying the comparison between right and left eye RNFL it was shown that only nasal and temporal RNFL quadrants have significant difference being thicker in right than in left eyes giving a similar results to Christiane Al-Haddad et al. [35] and this may also be attributed to the laterality and hemispheric dominance of the brain [36]. While when each eye was examined separately there was no statistically difference in the average RNFL and the four quadrants thickness in between the three groups.

The three groups of the study all follow the ISNT rule regarding the thickest to thinnest location and this is similar to other study conducted on RNFL thickness [21].

The limitation of the study was that the number of subjects in the hypermetropic group was thirty and this was less than the number for mild myopia and emmetropia, this is due to variability in distribution of hypermetropia with age since it mostly manifest after the age of 40. The refractive error taken in the study was only of mild degrees so we cannot know the variability of the study finding with higher degrees. Also the study incorporate an age range from 18 to 40 only so there is no wide age range to study whether there will be changing with age regarding RNFL thickness.

6. Conclusion

There is no significant difference in average peripapillary RNFL and the four quadrants thickness between the three study groups. And the spherical equivalent also has no significant correlation with the average RNFL and the four quadrants thickness. The axial length show negative correlation with RNFL thickness but this was insignificant. While axial length showed a negative correlation with nasal RNFL quadrants in myopic group while the hypermetropic group had a significant negative correlation in both inferior and temporal quadrants regarding axial length and RNFL quadrants thickness. The age shows a significant negative correlation in average RNFL and nasal RNFL quadrants thickness in emmetropic group, and significant negative correlation in nasal RNFL quadrants thickness in hypermetropic group.

Ethical issue

None.

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None.

Conflicts of interest

No conflicts of interest exist to declare.

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