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Effect of error of refraction and axial length on peripapillary retinal nerve fiber layer thickness in normal people and glaucomatous patients using optical coherence tomography

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Abstract

Background: The measurement of retinal nerve fibre layer (RNFL) thickness is widely recognized as a very delicate tool of optic nerve damage, since it manifests before the manifestation of visual field impairment.

Aim of the work: The aim of this study was to evaluate the effect of refractive status and axial length of the eye on the thickness of the peripapillary RNFL in individuals with and without glaucoma. This was achieved via the use of optical coherence tomography.

Methods: This research was carried on 54 eyes of 27 glaucomatous patients and 54 eyes of 27 healthy. Inclusion criteria were participants aged 20-60 years old, with clear ocular media and Glaucomatous patients were previously diagnosed by fundus examination, IOP measurement and visual field.

Results: The thickness of the RNFL in different quadrants is influenced by factors such as axial length, refractive error, and age. However, it has been discovered that changes in axial length or age do not have an impact on the thickness of the RNFL in the temporal quadrant, unlike the other quadrants. Multivariate analysis show that axial length and age are the main factors affecting RNFL thickness in myopic eyes either normal or glaucomatous.

Conclusions: The diagnosis of glaucoma with myopia is a controversy due to the alterations in the optic disc. This research used an OCT technology to evaluate the effect of axial length and refractive error on RNFL thickness. The findings revealed that changes in axial length had a differential effect, with the exception of the temporal quadrant. The presence or severity of changes in the temporal quadrant is often minimal or nonexistent. The thinning in the temporal quadrant may indicate the glaucoma.

Keywords: Error of refraction, axial length, peripapillary RNFL thickness, glaucomatous patients, OCT

Introduction

The thickness of the retinal nerve fibre layer (RNFL) is considered a very delicate mark of optic nerve injury in individuals with glaucoma, since it often occurs prior to the onset of visual field loss [1].

Several variables, including as age, sex, axial length, optic disc size, refractive status, and race, may have an impact on the thickness of the RNFL [2]. While red-free fundus ophthalmoscopy and photography provide direct imaging of the RNFL, it is important to note that these methods currently lack objectivity and quantifiability, since they are subjective and qualitative in nature. Consequently, they do not provide the means for quantitative assessment of RNFL thickness [3].

Optical Coherence Tomography (OCT) is a novel non-invasive technique that offers high-resolution cross-sectional imaging of various ocular structures. It is noteworthy for its impressive axial resolution of 10 microns. The measurement and visualization of the thickness of the retina, namely the RNFL, may be achieved by the use of high-resolution OCT [4]. Glaucoma is distinguished by an initial effect on the thickness of the RNFL, which is then followed by a subsequent and permanent advancement of incision in the optic disc and the emergence of irregularities in the visual field. Therefore, aprecise and dependable assessment of RNFL thickness, together with an understanding of the established ranges of normal RNFL thickness, has significant therapeutic value in the timely detection and ongoing surveillance of glaucoma.

While the thinning of the RNFL is considered an indication of glaucomatous damage, there is still uncertainty on whether the thickness of the RNFL varies depending on the refractive state of the eye. Therefore, it is essential to conduct an investigation to determine the presence of a connection between RNFL measures and axial length or refractive error [5]. Numerous research have been conducted to investigate the influence of axial length or refractive status on the thickness of the RNFL covering the optic nerve, using high-resolution spectral-domain OCT. These studies have suggested that when evaluating patients for the diagnosis and monitoring of glaucoma using OCT findings, it is important to consider the patient's axial length [4].

The research conducted an observation which found that eyes with myopia and longer axial length had a decreased average thickness of the peripapillary retinal nerve fiber layer. Conversely, eyes with hypermetropia and shorter axial length shown an increased thickness as compared to eyes with emmetropia [6].

The primary purpose of this work was to assess the impact of axial length and refractive status on peripapillary thickness of RNFL in both individuals without glaucoma and those diagnosed with glaucoma. This assessment was conducted using OCT and included a comparison between the two groups.

Methods and Patients

This study was carried on 54 eyes of 27 glaucomatous patients and 54 eyes of 27 healthy non glaucomatous age matched subjects. Patients were selected from the outpatient clinic and glaucomatous clinic of Mansoura Ophthalmology Hospital during the period from October 2020 to October 2021. The research study received ethical clearance from the Local Research Ethics Committee of the Faculty of Medicine, Tanta University, located in Egypt. All research participants provided informed consent. The researchers got an informed written agreement from either the patient or the families of the patients.

Inclusion criteria were participant’s age 20-60 years old, with clear ocular media and Glaucomatous patients from glaucoma clinic were previously diagnosed by fundus examination, IOP measurement and visual field.

Exclusion criteria were presence of systemic diseases or condition that might affect RNFL thickness other than glaucoma in glaucomatous patient as DM and hypertension, presence of neurological disease, those with amblyopia, strabismus, and corneal disorders, history of ocular trauma, previous refractive surgery and intraocular surgical intervention.

The study included 2 groups, divided as follows:

Group A: 54 glaucomatous eyes.

Group B: 54 non glaucomatous eyes (normal group).

The normal group consisted of individuals who did not have a history of ocular injuries, intraocular surgery, or systemic disorders, and who had normal results on ophthalmic examination. Both groups were divided into three subgroups (emmetrope, myope and hypermetrope). Each subgroup included 18 eyes.

The following were applied to all research participants as part of the protocol:

Comprehensive research: Information about yourself, such as your name, age, gender, profession, city of residence, etc.

Present disease history including symptoms, progression, and length of time affected, and Prior eye illness or surgery history.

Full ophthalmic examination: Visual acuity assessment, including uncorrected visual acuity (UDVA) and Best Corrected Visual Acuity (BCVA) was measured on a Snellen chart and was converted into the Log MAR. Manifest and cycloplegic refraction, Routine ophthalmologic examination using Slit lamp, Fundus examination by 90D lens, and IOP measurements using Goldman applanation tonometer.

(III) Axial lens measurement: This was performed using a scan ultrasound biometry (sonomed Pas Scan plus 300A, Escalon Medical Corp, USA). In most cases, a 10-MHz acoustic wave transducer is used for the A-scan ultrasound measurement of axial length. Resolution of 200 m and accuracy of 150 m are used to measure the distance along the optical axis among the internal limiting membrane of the retina and the anterior corneal vertex [7]. This procedure involves touching the cornea with a probe after applying a topical local anaesthetic.

(IV) OCT for measuring the thickness of the peripapillary RNFL: The OCT device was used to do this. One such instrument is the cirrus 5000HD-zeissOCT (Carl Zeiss Meditec, Inc., Dublin, CA, USA), which can do 2 mm of depth scanning at an A-scan velocity of 27.000 scans per second. The axial resolution is 5 m. Light at a wavelength of 840 nm is used by the device. The eye movement tracking and motion artifact reduction was performed using the FAST trac eye tracking system. Signal strengths of 6 or above were utilized for all scans [8].

All research participants gave their informed permission before undergoing any spectral domain OCT imaging procedures.

All study subjects were dilated with tropicamide 1% eye drops (BY Alexandria Co. for pharmaceuticals chemical industries, Alexandria – Egypt) before examination.

The target retinal region is scanned using a chosen scanning procedure, and the results are shown in a real-time OCT window. In order to properly place the scan, the individual was instructed to gaze at an internal fixation target. Retinal fixation is automatically maintained by the eye tracking technology. The OCT picture displays on the screen after the fundus image has been brought into focus by adjusting for refractive errors [9]. A properly aligned OCT picture will have the reference scan pattern centred on the region of interest. To maximize transmission strength, align the light source with the centre of the pupil. The measurement of RNFL thickness was conducted by using a circular scan with a diameter of 3.4 mm, which was centered at the optic disc head. This measurement was performed utilizing the RNFL thickness scan map. The retinal nerve fiber layer (RNFL), which is distinguished by its strong reflectivity signal, may be seen as the first layer showing in a red hue on the scan. The peripapillary RNFL was evaluated throughout the concentric circle of the optic disc border, and the thickness of the four areas (temporal, superior, inferior, and nasal quadrants) was measured. As per the source cited [9], The OCT scans that were preserved underwent both qualitative and quantitative analysis [9].

Statistical analysis

The data were inputted into the computer and subjected to analysis using version 20.0 of the IBM SPSS software program, developed by IBM Corp. The process of quantifying qualitative data included assigning numerical values and expressing them as percentages. The evaluation of the distribution's normalcy was performed by the use of the Kolmogorov-Smirnov test. The quantitative data were analyzed by using essential statistical measures, such as the range, which encompasses both the lowest and maximum values, as well as the mean and standard deviation. The statistical significance of the acquired findings was assessed by using a significance level of 5%. The provided text is of insufficient length to be edited academically. The chi-square test was used to examine categorical data and assess the discrepancies across many groups. The statistical technique used in this research was the student t-test, which was applied to compare two separate groups with respect to quantitative variables that had a normal distribution. The Mann-Whitney test was used to compare two groups under investigation within the context of quantitative data that had non-normal distribution. The Pearson correlation coefficient was used to assess the relationship between two variables that have a normal distribution. The F-test, which is often referred to as analysis of variance, was used to assess normally distributed quantitative variables in order to compare several groups. Moreover, to conduct pairwise comparisons, a Post Hoc test, namely the Tukey test, was used.

The Kruskal-Wallis test was used to analyze quantitative data with a non-normal distribution. The current study used this assessment tool to assess the disparities across many groups that were the primary subjects of inquiry. Moreover, within the framework of paired comparisons, the statistical technique referred to as Dunn's multiple comparisons test was used as a Post Hoc test.

Cases

- The patient under consideration is a 50-year-old male individual.
- The eyes affected by myopic glaucoma on both sides.
- The individual exhibits a spherical equivalent of -5.25 D in the right eye and -4.75 D in the left eye.
- The BCVA in the right eye was measured to be 0.6 LogMar, whereas in the left eye it was recorded as 0.5 LogMar.
- The IOP was measured to be 18 mm/Hg in the right eye and 16 mm/Hg in the left eye.
- The measurements for the right and left eye are 24.53 mm and 24.25 mm, respectively.
- Average RNFL thickness: 67µ and 73µ in right and left eye respectively.

Fig 1: A-scan ultrasound in both eyes of case (1).

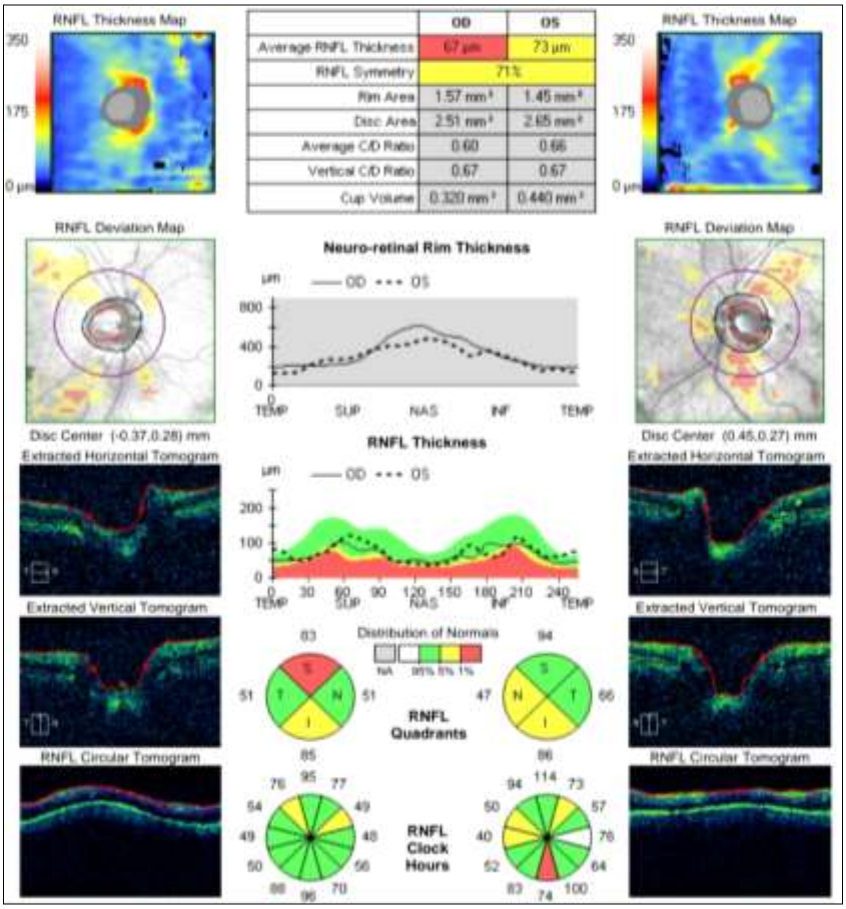

Fig 2: Peripapillary RNFL thickness measurement of both eyes in case (1) by OCT: showed decrease of average RNFL thickness of both eyes and thinning in superior and inferior quadrant of right eye and nasal and inferior quadrant of left eye.

Results

As regards age and sex

There was a lack of significant difference observed among the patient characteristics of both groups throughout the three subgroups. Table 1

Table 1: Comparison between 2 groups and patient characters

	Emmetrope		**Myope**		**Hypermetrope**	
Age	**Glaucomatous (n = 9)**	**Normal (n = 9)**	**Glaucomatous (n = 9)**	**Normal (n =9)**	**Glaucomatous (n = 9)**	**Normal (n=9)**
Min. – Max.	32.0 – 59.0	28.0 – 60.0	33.0 – 60.0	22.0 – 60.0	30.0 – 60.0	26.0 – 59.0
Mean±SD.	45.89±9.39	39.44±10.45	49.44±8.64	45.17±12.76	49.06±8.61	42.28±11.57
T	1.946		1.177		1.994	
P	0.060		0.247		0.055	
	Glaucomatous (n = 27patients)			Normal (n = 27 patients)		
	Emmetrope (n= 9)	Myope (n= 9)	Hypermetrope (n= 9)	Emmetrope (n= 9)	Myope (n= 9)	Hypermetrope (n= 9)
F	0.867			1.089		
P	0.426			0.344		
	Emmetrope		Myope		Hypermetrope	
	Glaucomatous	Normal	Glaucomatous	Normal)	Glaucomatous	Normal
Sex						
Male	4 (44.5%)	3 (33.5%)	4 (44.4%)	2 (22.2%)	5 (55.6%)	3 (33.4%)
Female	5 (55.5%)	6 (66.5%)	5 (55.6%)	7 (77.8%)	4 (44.4%)	6 (66.6%)
χ^2	0.450		2.00		2.857	
P	0.502		0.157		0.091	
	Glaucomatous (n = 54)			Normal (n = 54)		
	Emmetrop	Myope	Hypermetrope	Emmetrope	Myope	Hypermetrope
χ^2	0.444			1.243		
P	0.801			0.537		

As regards IOP

The current study showed that in comparison between glaucomatous and normal group there was statically Signiant higher IOP in hypermetropic and emmetropic glaucomatous subgroups than the normal group with $p<0.001$, $p<0.004$ respectively.

Also, in the normal group, myopic and hypermetropic subgroups had a significant higher IOP than emmetropic ones with $p<0.001$.Table (2)

Table 2: Comparison between 2 groups and IOP in each subgroup. N.B: All glaucomatous patients from hospital glaucoma clinic were under ant glaucomatous treatment such as b blockers and prostaglandin analogue, so IOP was controlled.

	Emmetrope		**Myope**		**Hypermetrope**	
	Glaucomatous (n = 18)	**Normal (n = 18)**	**Glaucomatous (n = 18)**	**Normal (n = 18)**	**Glaucomatous (n = 18)**	**Normal (n = 18)**
IOP (mm/Hg)						
Min. – Max.	15.0 – 24.0	12.0 – 15.0	12.0 – 23.0	13.0 – 18.0	13.0 – 22.0	12.0 – 18.0
Mean±SD.	18.44±2.23	13.33±0.91	17.11±3.51	16.0±1.41	17.11±2.54	14.89±1.68
T	9.011		1.245		3.097*	
P	<0.001*		0.226		0.004*	
	Glaucomatous (n = 54)			Normal (n = 54)		
	Emmetrope (n = 18)	Myope (n = 18)	Hypermetrope (n = 18)	Emmetrope (n = 18)	Myope (n = 18)	Hypermetrope (n = 18)
IOP (mm/Hg)						
Min. – Max.	15.0 – 24.0	12.0 – 23.0	13.0 – 22.0	12.0 – 15.0	13.0 – 18.0	12.0 – 18.0
Mean±SD.	18.44±2.23	17.11±3.51	17.11±2.54	13.33±0.91	16.0±1.41	14.89±1.68
F	1.347			17.197		
P	0.269			<0.001*		
Sig. bet. Subgrps.	–			p_1<0.001*,p_2=0.004*,p_3=0.048*		

SD: Standard deviation, t: Student t-test

As regards the axial length

The research demonstrated that in 2 groups, there was a significant shorter axial length in the hyperopic subgroup (with mean AL 21.86 mm), and longer in the myopic subgroup (with mean AL 24.01) mm than the emmetropic subgroup (with mean AL 22.8 mm). There were also significant differences between the emmetropic and myopic groups, the emmetropic and hypermetropic groups, and the myopic and hypermetropic groups, as well as between the glaucomatous and control groups. Differences between the myopic and emmetropic groups in the control group were significant (p2<0.001*), as were differences between the emmetropic and hypermetropic groups. Additionally, substantial differences were found between the myopic and hypermetropic groups. Table (3)

Table 3: Comparison between 2 groups and axial length in each subgroup

Axial length (mm)	Emmetrope		Myope		Hypermetrope	
	Glaucomatous (n = 18)	Normal (n = 18)	Glaucomatous (n = 18)	Normal (n = 18)	Glaucomatous (n = 18)	Normal (n = 18)
Min. – Max.	22.60 – 23.20	22.40 – 23.20	23.20 – 24.80	23.30 – 24.80	21.30 – 22.50	21.20 – 22.50
Mean±SD.	22.86±0.21	22.82±0.26	23.78±0.47	24.01±0.47	21.97±0.41	21.86±0.39
T	0.491		1.449		0.869	
P	0.627		0.156		0.391	

	Glaucomatous (n = 54)			Normal (n = 54)		
	Emmetrope (n = 18)	Myope (n = 18)	Hypermetrope (n = 18)	Emmetrop (n = 18)	Myope (n = 18)	Hypermetrope (n = 18)
Min. – Max.	22.60 – 23.20	23.20 – 24.80	21.30 – 22.50	22.40 – 23.20	23.30 – 24.80	21.20 – 22.50
Mean±SD.	22.86±0.21	23.78±0.47	21.97±0.41	22.82±0.26	24.01±0.47	21.86±0.39
F	100.126			142.390		
P	$<0.001^*$			$<0.001^*$		
Sig. bet. Subgrps.	$p_1<0.001^*,p_2<0.001^*,p_3<0.001^*$			$p_1<0.001^*,p_2<0.001^*,p_3<0.001^*$		

p: p value for comparing between the studied subgroups
p_1: p value for comparing between Emmetrope and Myope
p_2: p value for comparing between Emmetrope and Hypermetrope
p_3: p value for comparing between Myope and Hypermetrope

As regards error of refraction:
In emmetropic group, the mean Error of refraction was 0.08±0.24D (range -0.25D to+0.25D) in glaucomatous patients, and 0.0±0.26 D (range -0.25D to 0.25D) in normal people with no significant differences between 2 groups (p: 0.462). As regard myopic group, the mean Error of refraction was -2.75±-2.75 D (range -6.0 D to -0.50 D) in glaucomatous patients, and -3.14±1.63 D (range -6.0 D to-0.50D) in normal people with no significant differences between the 2 groups (p: 0.462). In the hyperopic group, the mean Error of refraction was 2.10±0.95 D (range + 0.50 D to +4.50 D) in glaucomatous patients, and 2.65±1.12 D (range +0.50 D to +4.50 D) in normal people with no significant differences between 2 groups (p: 0.097).
In glaucomatous group under treatment, the mean Error of refraction was 0.08±0.24 D(range -0.25D to+ 0.25D), -2.75±-2.75 D (range -6.0D to-0.50D), and 2.10±0.95 D (range +0.50 D to +4.50 D) in emmetropic, myopic, and hyperopic people respectively, with statistically significant differences between emmetropic and myopic groups (p_1:0.001*), between emmetropic and hypermetropic groups (p_2:0.001*), and myopic and hypermetropic groups ($p_3<0.001^*$). In normal group, the mean Error of refraction was 0.0±0.26 D (range -0.25D to+ 0.25D), -3.14±1.63 D (range -6.0D to-0.50D), and 2.65±1.12 D (range +0.50D to +4.50D) in emmetropic, myopic, and hyperopic people respectively, with statistically significant differences among myopic and emmetropic groups (p_1:0.001*), between emmetropic and hypermetropic groups (p_2:0.001*), and myopic and hypermetropic groups ($p_3<0.001^*$).

Table 4: Comparison between 2 groups and error of refraction (spherical equivalent) in each subgroup:

Error of refraction (D)	Emmetrope		Myope		Hypermetrope	
	Glaucomatous (n = 18)	Normal (n = 18)	Glaucomatous (n = 18)	Normal (n = 18)	Glaucomatous (n = 18)	Normal (n = 18)
Min. – Max.	-0.25 –+ 0.25	-0.25 –+ 0.25	-6.0 – -0.50	-6.0 – -0.50	0.50 – +4.50	0.50 – +4.50
Mean±SD.	0.08±0.24	0.0±0.26	-2.75±-2.75	-3.14±1.63	2.10±0.95	2.65±1.12
U	138.00		138.50		109.00	
P	0.462		0.462		0.097	

	Glaucomatous (n = 54)			Normal (n = 54)		
Error of refraction (D)	Emmetrope (n = 18)	Myope (n = 18)	Hypermetrope (n = 18)	Emmetrope (n = 18)	Myope (n = 18)	Hypermetrope (n = 18)
Min. – Max.	-0.25 – 0.25	-6.0 – -0.50	0.50 – 4.50	-0.25 – 0.25	-6.0 – -0.50	0.50 – 4.50
Mean±SD.	0.08±0.24	-2.75±-2.75	2.10±0.95	0.0±0.26	-3.14±1.63	2.65±1.12
H	47.761*			47.513		
P	$<0.001^*$			$<0.001^*$		
Sig. bet. Subgrps.	$p_1=0.001^*,p_2=0.001^*,p_3<0.001^*$			$p_1=0.001^*,p_2=0.001^*,p_3<0.001^*$		

p: p value for comparing between the studied subgroups
p1: p value for comparing between Emmetrope and Myope
p2: p value for comparing between Emmetrope and Hypermetrope
p3: p value for comparing between Myope and Hypermetrope

As regards RNFL thickness
In glaucomatous group
Our study showed that in glaucomatous group average RNFL was significantly higher in hyperopic and lower in myopic than emmetropic subgroup. Thinning in myopic subgroup in inferior and nasal quadrants is more than emmetropic subgroup while there was no difference in superior and temporal quadrants thinning in different subgroups of glaucoma.
The average RNFL thickness in the superior quadrant was 107.2±11.39 µm, 95.28±24.75 µm, and 104.1±18.68 µm in the emmetrope, myope and hypermetrope groups respectively with no significant differences between the groups (p: 0.161). The average RNFL thickness in the inferior quadrant was 106.8±13.12 µm 90.78±22.69 µm, and 98.0±16.71 µm in the emmetrope, myope and hypermetrope groups respectively with significant differences among emmetrope and myope (p1=0.027*). The average RNFL thickness in the nasal quadrant was 68.94±8.78 µm, 57.27±17.13 µm and 73.55±16.22 µm in the emmetrope, myope and hypermetrope groups respectively with significant differences among the groups (p= 0.005*),

between emmetrope and myope (p1=0.051*), and between myope and hypermetrope (p3=0.004*). The average RNFL thickness in the temporal quadrant was 67.50±8.87 µm, 62.00±8.46 µm, and 63.88±5.26 µm in the emmetrope, myope and hypermetrope groups respectively with no significant differences between three subgroups. The average RNFL thickness showed a mean of 90.28±3.79 µm, 78.11±6.91 µm, and 86.11±6.91 µm in the emmetrope, myope and hypermetrope respectively with statistically significant differences between emmetrope and myope groups (p1<0.001*), and between myope and hypermetrope (p3=0.001*).

In Normal group

Our study showed that in normal group average RNFL, nasal superior and inferior quadrants were significantly higher in hypermetropic and lower in myopic than emmetropic subgroups.

The average RNFL thickness in the superior quadrant was 114.5±8.80 µm, 108.0±8.22 µm, and 124.6±12.75 µm in the emmetrope, myope and hypermetrope groups respectively with significant differences between emmetrope and myope (p=0.042*), Emmetrope and Hypermetrope (p_2=0.012*), and between Myope and Hypermetrope (p_3<0.001*). The average RNFL thickness in the inferior quadrant was 122.6±11.21 µm, 112.0±25.91 µm, and 130.6±8.15 µm in the emmetrope, myope and hypermetrope groups respectively with statistically significant differences between emmetrope and myope(p_1=0.040*), emmetrope and hypermetrope (p_2=0.034*) and between Myope and Hypermetrope groups (p_3=0.005*). The mean RNFL thickness in the nasal quadrant was 76.16±11.31 µm, 67.61±8.52 µm, and 84.72±11.198 µm in the emmetrope, myope and hypermetrope groups respectively with significant differences between emmetrope and myope groups (p_1=0.034*), emmetrope and hypermetrope (p_2=0.045) and between Myope and Hypermetrope groups (p_3<0.001*). The mean RNFL thickness in the temporal quadrant was 72.44±10.06 µm, 65.77±9.69 µm, and 73.44±12.6µm in the emmetrope, myope and hypermetrope groups respectively with no significant differences between three subgroups. The average RNFL thickness showed a mean of 99.56±3.26 µm, 88.78±4.77 µm, and 105.17±3.78 µm in the emmetrope, myope and hypermetrope respectively with significant differences between emmetrope and myope groups p_1<0.001*), between emmetrope and hypermetrope (p_2<0.001*), and between myope and hypermetrope (p_3<0.001*). Table (5)

Table 5: Comparison between the two studied groups according to peripapillary RNFL thickness in each subgroup

RNFL Thickness (µ)	Glaucomatous (n = 54)			Normal (n = 54)		
	Emmetrope (n = 18)	Myope (n = 18)	Hypermetrope (n = 18)	Emmetrope (n = 18)	Myope (n = 18)	Hypermetrope (n = 18)
Superior						
Min. – Max.	90.0 – 129.0	60.0 – 149.0	67.0 – 149.0	99.0 – 125.0	96.0 – 125.0	109.0 – 155.0
Mean±SD.	107.2±11.39	95.28±24.75	104.1±18.68	114.5±8.80	106.0±8.22	124.6±12.75
F	1.895			12.219*		
P	0.161			<0.001*		
Sig. bet. Subgrps.	–			p_1=0.042*, p_2=0.012*, p_3<0.001*		
Inferior						
Min. – Max.	84.0 – 131.0	46.0 – 122.0	61.0 – 125.0	104.0 – 145.0	14.0 – 134.0	119.0 – 144.0
Mean±SD.	106.8±13.12	90.78±22.69	98.0±16.71	122.6±11.21	112.0±25.91	130.6±8.15
F	3.588*			5.419*		
P	0.035*			0.007*		
Sig. bet. Subgrps.	p_1=0.027*, p_2=0.315, p_3=0.454			p_1=0.040*, p_2=0.034*, p_3=0.005*		
Nasal						
Min. – Max.	60.0 – 86.0	43.0 – 109.0	52.0 – 117.0	57.0 – 93.0	55.0 – 83.0	68.0 – 108.0
Mean±SD.	68.9±8.78	57.27±17.13	73.55±16.22	76.16±11.316	67.22±8.52	84.72±11.19\
F	5.994			12.681		
P	0.005*			<0.001*		
Sig. bet. Subgrps.	p_1=0.051*, p_2=0.611, p_3<0.004*			p_1=0.034*, p_2=0.045*, p_3<0.001*		
Temporal						
Min. – Max.	57.0 – 84.0	49.0 – 74.0	54.0 – 75.0	57.0 – 90.0	44.0 – 81.0	52.0 – 90.0
Mean±SD.	67.50±8.87	62.50±8.46	63.88±5.26	72.44±10.06	65.77±9.69	73.44±12.6
F	2.367			2.731		
P	0.104			0.075		
Sig. bet. Subgrps.	–			–		
Average RNFL Thickness						
Min. – Max.	84.00 – 97.00	68.00 – 91.00	74.00 – 98.00	95.00 – 105.00	80.00 – 95.00	99.00 – 111.00
Mean±SD.	90.28±3.79	78.11±6.91	86.11±6.91	99.56±3.26	88.78±4.77	105.17±3.78
F	18.797*			78.618*		
P	<0.001*			<0.001*		
Sig. bet. Subgrps.	p_1<0.001*, p_2=0.107, p_3=0.001*			p_1<0.001*, p_2<0.001*, p_3<0.001*		

p: p value for comparing between the studied subgroups

p_1: p value for comparing between Emmetrope and Myope

p_2: p value for comparing between Emmetrope and Hypermetrope

p_3: p value for comparing between Myope and Hypermetrope

Correlation between error of refraction and peripapillary RNFL thickness

In glaucomatous group

No significant connection was found among the thickness of the RNFL and the error of refraction in any of the quadrants within the emmetropic subgroup. Significant and important correlations were found between the severity of refractive error and the thickness of the RNFL in the superior and inferior quadrants, as well as the average thickness of the RNFL in the small sample under study. Refractive error and inferior RNFL thickness were shown to be significantly positively correlated in the hypermetropia subgroup

In normal group

A lack of significant correlation was seen among the magnitude of refractive error and the thickness of the RNFL in all quadrants among those classified as emmetropic. In the present study, a noteworthy and significant positive correlation was seen between refractive error and RNFL thickness in the superior and nasal quadrants, as shown by the myopic sample.

A significant positive correlation was seen in the hypermetropic subgroup between refractive error and RNFL thickness in the inferior and nasal quadrants, in addition to the average RNFL thickness. Table (6)

Table 6: Correlation between Error of refraction, and peripapillary RNFL thickness in each group

		Error of refraction vs. RNFL									
	No.	Superior		Inferior		Nasal		Temporal		Average	
		R	P	R	P	r	P	R	p	R	P
Glaucomatous	54										
Emmetrope	18	0.376	0.124	-0.290	0.244	0.234	0.287	-0.437	0.070	0.214	0.395
Myope	18	0.568	0.014*	0.568	0.014*	-0.138	0.585	-0.143	0.570	0.781	<0.001*
Hypermetrope	18	-0.116	0.646	0.553	0.017*	-0.154	0.543	-0.206	0.413	0.148	0.558
Normal	54										
Emmetrope	18	-0.114	0.651	-0.243	0.332	0.255	0.308	0.287	0.247	0.315	0.202
Myope	18	0.589	0.010*	0.465	0.050	0.560	0.016*	0.051	0.841	0.963	<0.001*
Hypermetrope	18	0.280	0.260	0.493	0.039*	0.695	0.001*	0.331	0.180	0.934	<0.001*

Correlation between axial length and peripapillary RNFL thickness

In glaucomatous group

Within the emmetropic subgroup, a notable absence of a substantial association was seen between the axial length and RNFL thickness across all quadrants. Within the myopic subgroup, a noteworthy inverse relationship was observed between the axial length and the thickness of the RNFL in the superior and inferior quadrants, as well as in the average thickness. Within the hypermetropic subgroup, a notable inverse relationship was observed between the axial length and the thickness of the RNFL in the superior and nasal quadrants, as well as in the average thickness.

In normal group: Within the standard group, specifically in the emmetropic subgroup, there was no significant association observed among the length of the eye's axial dimension and the thickness of the RNFL in any of the quadrants. Within the myopic subgroup, a notable inverse relationship was seen between the length of the eye's axial dimension and the thickness of the RNFL in the superior, inferior, and nasal quadrants. Within the hypermetropic subgroup, a noteworthy inverse relationship was observed between the axial length and the thickness of the RNFL in both the superior and inferior quadrants. Table (7)

Table 7: Correlation axial length and peripapillary RNFL thickness in each group

		Axial length vs. RNFL									
	No.	Superior		Inferior		Nasal		Temporal		Average	
		R	P	R	P	R	P	R	P	R	P
Total Glaucomatous	54										
Emmetrope	18	0.236	0.346	0.052	0.839	0.133	0.600	0.166	0.511	0.088	0.727
Myope	18	-0.553	0.017*	-0.553	0.017*	0.159	0.528	0.180	0.475	-0.765	<0.001*
Hypermetrope	18	-0.478	0.045*	-0.300	0.227	-0.493	0.038*	-0.044	0.863	-0.583	0.011*
Total Normal	54										
Emmetrope	18	0.064	0.800	0.356	0.147	-0.405	0.096	-0.392	0.108	-0.435	0.071
Myope	18	-0.637	0.004*	-0.462	0.050*	-0.562	0.015*	-0.331	0.180	-0.976	<0.001*
Hypermetrope	18	-0.493	0.038*	-0.512	0.030*	-0.144	0.570	-0.216	0.390	-0.498	0.035*

Correlation between age and peripapillary RNFL thickness

In glaucomatous group

Only the RNFL in the superior quadrant is negatively correlated with age in the emmetropic subgroup. Age inversely correlated with RNFL thickness in the superior quadrant and overall, in the myopic subgroup.

Age correlated negatively with RNFL only in the superior quadrant in the hypermetropic sample.

In normal group

Within the emmetropic subgroup, a statistically significant negative connection was seen between age (measured in years) and RNFL thickness in the superior and nasal quadrants, as well as in the average thickness. Within the myopic subgroup, a notable inverse relationship was seen between the age of individuals in years and the RNFL measurements in the superior and temporal quadrants, as well as the average RNFL thickness. Within the hypermetropic subgroup, our analysis revealed no statistically significant association between age (measured in years) and RNFL thickness in either of the quadrants or in the average thickness. Table (8)

Multivariate analysis

Multivariate analysis show that axial length and age are the main factors affecting RNFL thickness in myopic glaucomatous eyes.

Multivariate analysis showed that axial length and age are the main factors affect retinal nerve fiber layer thickness in normal myopic people.

Multivariate analysis show that axial length is the main factor affect retinal nerve fiber thickness in normal hypermetropic people. Table (9).

Table 8: Correlation between age (years) and peripapillary RNFL thickness in each group:

		Age (years) vs. RNFL									
	No.	**Superior**		**Inferior**		**Nasal**		**Temporal**		**Average**	
		R	**P**	**r**	**P**	**R**	**p**	**r**	**P**	**R**	**p**
Total Glaucomatous	54										
Emmetrope	18	-0.430	0.058*	0.064	0.800	-0.041	0.873	0.369	0.132	0.112	0.659
Myope	18	-0.472	0.029*	-0.406	0.094	-0.255	0.308	-0.047	0.853	-0.797	<0.001*
Hypermetrope	18	-0.609	0.007*	-0.348	0.157	0.309	0.212	0.023	0.929	-0.344	0.162
Total Normal	54										
Emmetrope	18	-0.564	0.015*	-0.376	0.124	-0.559	0.016*	0.130	0.607	-0.664	0.003*
Myope	18	-0.622	0.006*	-0.045	0.859	-0.258	0.301	-0.509	0.031*	-0.491	0.039*
Hypermetrope	18	-0.335	0.174	-0.272	0.274	0.288	0.246	-0.031	0.903	-0.315	0.203

r: Pearson coefficient

Table 9: Univariate and multivariate linear regression analysis for the parameters affecting average RNFL thickness in myopic Glaucomatous eyes, in hypermetropic Glaucomatous eyes, in myopic eyes of normal people and in hypermetropic eyes of normal people

Myopic glaucomatous subgroup	**Univariate**		**#Multivariate**	
	p	**B (95%C.I)**	**P**	**B (95%C.I)**
Axial length	<0.001*	-11.134 (-16.103–-6.164)	0.004*	10.448 (-10.645–31.541)
Age	<0.001*	-0.637 (-0.893–0.382)	0.005*	-0.346 (-0.567–-0.125)
Error refraction	<0.001*	3.714 (2.139–5.289)	0.226	4.063 (-2.851–10.977)
Hypermetropic glaucomatous subgroup	Univariate		#Multivariate	
	P	B (95%C.I)	P	B (95%C.I)
Axial length	0.011*	-10.270(-17.851—2.689)		
Age	0.162	-0.277 (-0.676– 0.123)		
Error refraction	0.558	1.076 (-2.731–4.882)		
Myopic normal subgroup	Univariate		#Multivariate	
	P	B (95%C.I)	p	B (95%C.I)
Axial length	<0.001*	-9.442 (-11.122–-8.762)	0.042*	-6.515 (-12.773– 0.259)
Age	0.039*	-0.184 (-0.356 – -0.011)	0.021*	-0.117 (-0.213–-0.021)
Error refraction	0.001*	1.619 (0.321–2.917)	0.906	-0.052 (-0.978– 0.875)
Hypermetropic normal subgroup	Univariate		#Multivariate	
	P	B (95%C.I)	P	B (95%C.I)
Axial length	0.035*	-4.805 (-9.236–-0.373)	0.035*	-3.017 (-5.785–-0.249)
Age	0.203	-0.103 (-0.267– 0.061)		
Error refraction	0.001	3152(2.511-3.794)	0.576	3.968 (2.143–5.794)

B: Unstandardized Coefficients
C.I: Confidence interval, LL: Lower limit, UL: Upper Limit
#: All variables with $p<0.05$ was included in the multivariate

Discussion

Glaucoma is characterized by the first involvement of RNFL, followed by the subsequent development of irreversible optic disc excavation and visual field defects. Hence, the precise and dependable assessment of RNFL thickness, together with an understanding of its established ranges, has significant therapeutic value in the timely detection of glaucoma. While RNFL thickness is considered an indicator of glaucomatous damage, there is still a lack of certainty on whether variations in the refractive state of the eye would affect RNFL thickness. Hence, it is essential to examine if a link exists between the thickness of the RNFL and the axial length and refractive errors of the eye [2].

Numerous studies were done using OCT to detect the relation between RNFL thickness and axial length/spherical equivalent specially in myopia due to its association with primary open angle glaucoma, but in this research we aimed to show this relation in myopic, hypermetropic normal people and glaucomatous patients [1].

In this study we measured RNFL between 2 groups by OCT and compared between them.

The research also demonstrated that the glaucomatous group had a significant lower Best-corrected visual acuity (BCVA) when compared with the normal one in all the three subgroups.

This result is found to be matched with a study performed by Ahmed E. Abd EL-Naby *et al.*, [10] in which they evaluated retinal nerve fiber layer thickness in patients with glaucoma and reported that glaucomatous patients had statistically significant lower Best-corrected visual acuity (BCVA) than the control individuals.

The current study showed that in the normal group; myopic and hypermetropic subgroups had a significant higher IOP than emmetropic ones ($P_1<0.001$), ($P_2=0,004$) respectively.

This result is in accordance with a study by Hideki Nomura *et al.*, [3] who showed that IOP increased with the advancing degree of myopia, even after adjustment of age, central corneal thickness and other related factors. IOP of myopic people was significantly higher than that of emmetropic ones.

This result is also found to be matched with the study by Akshay Nayak *et al.*, [1] in which 104 myopic subjects, 140 hypermetropic ones and 100 emmetropic ones went full ophthalmic examination and the study found that myopic people had higher IOP than the emmetropic ones and thick cornea seen in hypermetropic people may lead to false high IOP reading.

The current study showed that in both groups, (normal and glaucomatous), there was a statistically significant shorter axial length in the hyperopic subgroup (with mean AL 21.86 mm), and longer in the myopic subgroup (with mean AL 24.01) mm than the emmetropic subgroup (with mean AL 22.8 mm) ($p<0.001$).

This result is compatible with the previous study by Liorente *et al.*, [11] in which they studied 24 myopic and 22 hyperopic eyes. They found that axial length was statistically significant shorter in hyperopic eyes and longer

in myopic ones than emmetropic eyes.
Strang *et al*., [12] also suggested that hyperopia is similar to myopia, predominantly axial in nature and revealed a significant relationship between the degree of hypermetropia and axial length.
The study also demonstrated that in the normal group there was a significant larger cup to disc ratio in the myopic subgroup and a statistically significant smaller cup to disc ratio in the hypermetropic one than emmetropic ones.
Jose Pablo *et al*., [13] reported similar results in his study in which they evaluated the prevalence of disc cupping in non-glaucomatous eyes and found that the diameter of the optic cup also varies widely among individuals The regions of the optic disc and optic cup are associated in normal eyes. The optic cup is bigger the larger the optic disc. There is a huge disk with a large cup in myopic eyes, and a tiny disc with a small cup in hypermetropic eyes.
The study also showed that there was a significant large cup to disc ratio in the glaucomatous patient in all subgroups more than in the normal group.
This result is also in agreement with a study performed by Sanfilippo *et al*., [14] in It included 80 glaucomatous patients and 80 normal individuals. The optic cup was assessed in glaucoma, and the results indicated that the cup to disc ratio is much higher in the glaucoma group than in the normal group, suggesting an early diagnosis.
The study showed that in the normal group: the mean peripapillary retinal nerve fiber layer thickness in emmetropic, hyperopic and myopic subgroups was 99.56±3.26 µm, 105.17±3.78 µm, and 88.78±4.77 µm respectively with ($p < 0.001$).
Retinal nerve fiber layer thickness was statistically significant thinner in the myopic subgroup in (superior, inferior and nasal quadrants) than the emmetropic one, with no statistically significant change in temporal quadrant. While in the hyperopic sub group retinal nerve fiber layer thickness was statistically significant thicker in superior, inferior and nasal quadrants than the emmetropic one, with no change in temporal quadrant.
This result is found to be matched with the study performed by Veysi Öner *et al*., [15] 154 healthy individuals were split into three groups: those with myopia, hyperopia, and emmetropic vision. The peripapillary RNFL thickness was assessed using the Stratus OCT. In the myopic group, the mean peripapillary RNFL was comparatively thinner than in the emmetropic group ($p < 0.05$). The superior and inferior quadrants had a thinner texture. Compared to the emmetropic group, the hyperopic group's RNFL was thicker in the nasal and inferior quadrants ($p < 0.05$).
Sang Hoon Park *et al*., [16] showed the same result as they studied 291 eyes of healthy subjects with different refractive states (emmetropic, myopic and hyperopic) and measurements of ocular biometric parameters were performed including RNFL thickness using OCT. Other parameters were: refractive error, axial length, central corneal thickness, anterior chamber depth, corneal curvature. According to this research, there was a trend toward myopia and reduced RNFL thickness in longer eyes, and a tendency toward hyperopia and increased RNFL thickness in shorter eyes.
This result is not compatible with a study performed by Yalcin and Balci, [17] in which they concluded that the mean RNFL thickness for hyperopic eyes was 101±10.77 µm and for emmetropic eyes was 105.08±10.10 µm. They revealed no statistically significant difference between these groups (P=0.285). This difference between our result and this result may be due to this study being done in children with age ranging from 8 to 14 years old, their axial length was not completely fixed and tend to change as the eye grows and their error of refraction is mainly lenticular not axial.
The current study showed that, in the glaucomatous group**:** the average RNFL thickness in emmetropic, myopic and hypermetropic subgroups was 90.28±3.78 µm, 78±6.78 µm and 86.11±6.91 µm respectively with a statistically significant difference between three subgroups ($p<0.001$). Myopic subgroup showed a statistically significant thinning in inferior and nasal quadrants more than that of emmetropic ones. Thinning in nasal quadrant of the myopic subgroup is statistically significant more than that in the hyperopic subgroup. There was no statistically significant difference in superior and temporal quadrant thickness between the three subgroups. This result is found to be matched with a study performed by Jost B. Jones *et al*., [18] who reported that optic disc morphology differed significantly in myopic glaucomatous eyes as there was more loss in the neuroretinal rim in myopic eyes with glaucoma than that of hyperopic and emmetropic ones with glaucoma.
Cinzia Coris *et al*., [19] investigated retinal nerve fiber layer thickness in hyperopic patients suffering from glaucoma. They divided into 3 groups (36 eyes of hyperopic glaucomatous patient, 24 eyes of normal hyperopic and 20 eyes of normal emmetropic people). The study showed results matched with the present study; retinal nerve fiber was significantly thicker in all hyperopic eyes than emmetropic due to effect of axial length, and there was a significant thinning in hyperopic glaucomatous eye.
This result is not matched with a study by Jin Young Lee *et al*., [20] in which there was a comparison of rates of retinal nerve fiber layer thinning between patient with non-myopic glaucoma and moderate myopic glaucoma and high myopic glaucoma among 231 glaucomatous eyes from 231 patients and they found that retinal nerve fiber thinning was not different among the glaucoma subgroups based on refractive error. However, sectoral retinal nerve fiber layer thinning showed significant difference. This difference between our result and this result may be due to different races as this study was done on Korean people, different sample size and long follow up duration in this study as it was 5 years.
The current study showed that glaucomatous patients had a statistically significant thinning in inferior, nasal quadrants and average retinal nerve fiber thickness when compared with the normal one in all the three subgroups.
This result is in coordination with a study by Ahmed E. Abd EL-Naby *et al*., [10] who evaluated retinal nerve fiber layer thickness changes in primary open angle glaucoma and showed that normal controls had significantly higher RNFl measurements when compared with all degrees of glaucoma especially in inferior quadrant and average thickness.
The current study showed that in the normal group there was a statistically significant negative correlation between axial length and retinal nerve fiber layer thickness. In myopic subgroup when axial length increased, superior, inferior, nasal quadrants and average thickness decreased. In hypermetropic subgroup when axial length decreased, superior, inferior quadrants and average retinal nerve fiber layer thickness increased.
This study also showed that in normal group there was significant positive correlation between error of refraction and retinal nerve fiber layer. In myopic subgroup: when errors of refraction decreased, superior, nasal quadrants and average retinal nerve fiber layer thickness decreased. In hypermetropic subgroup when error of refraction increased, inferior, nasal quadrants and average retinal nerve fiber layer thickness increased.

This study also showed that in normal group: There was a significant negative correlation between age and RNFL in myopic and emmetropic subgroups in superior and temporal quadrants, but this correlation is not statistically significant in hypermetrope ones.

This result is found to be matched with a study by Chau-Yin Chen *et al*., [21] The study conducted an evaluation on the impact of axial length and age on the thickness of the RNFL. The findings revealed a correlation between changes in RNFL thickness and age in the superonasal, superior, and temporal segments. Additionally, a correlation was observed between RNFL thickness and axial length in the non-temporal segments. These results are also compatible with a study by Delia Bendschenider *et al*., [22] in which peripapillary retinal nerve fiber layer of 170 healthy people was measured using optical coherence tomography, this study showed that mean retinal nerve fiber layer thickness was negatively correlated with age (p=0.005) and axial length (p=0.001) and positively correlated with refractive error ($p<0.001$).

Sonika Porwal *et al*., [23] reported the same results in their study in which they measured RNFL thickness in myopic people and found that there was a significant decrease RNFL thickness with an increase in error of refraction and grade of myopia, axial length and age. The research recommended careful analysis of RNFL data in myopic eyes with axial length equal or more than 24 mm because it could be wrongly diagnosed with glaucoma. Rauscher *et al*., [24] Furthermore, the study revealed a notable positive correlation between axial length and the average peripapillary RNFL thickness in the superior and inferior quadrants among individuals with myopia. However, a weaker correlation was observed between refractive error and RNFL thickness in both quadrants. The study consisted of a total of 27 participants, and it is posited that the limited sample size hindered the ability to derive any meaningful findings.

The results of the research demonstrated a strong negative connection between RNFL and axial length in the glaucomatous group. The thickness of the superior, inferior, and average RNFL reduced in the myopic subgroup as axial length rose. When axial length dropped, the average thickness of the RNFL and the superior nasal quadrants rose in the hypermetropic subgroup.

This research also shown a strong positive connection between RNFL and refraction error in the glaucomatous group. In the myopic sample, the average thickness of the retinal nerve fiber layer and the superior and inferior quadrants dropped as refraction errors decreased. When the hypermetropic subgroup's inferior nasal quadrant thickness grew, consequently did the refraction error.

This result is found to be matched with Sagar B. Patel *et al*., [25] the present study examined the relationship between axial length and RNFL in both normal individuals without glaucoma and patients diagnosed with glaucoma. A total of 170 eyes belonging to 89 persons were included in the analysis, with measurements of RNFL thickness and axial length obtained using OCT. The research observed a notable reduction in axial length across all quadrants in both the normal and glaucomatous groups, with the exception of the temporal quadrant which exhibited either nil or minimal non-significant thinning. There is no robust link seen between axial length and the temporal quadrant. However, the presence of a notable thinning in this region may elicit concern over the advancement of glaucoma.

The present research also shown a statistically significant inverse relationship between age and RNFL in the group of individuals with glaucoma. The observed link was shown to be present in the superior quadrant throughout the three categories, namely myopic, emmetropic, and hypermetropic. Additionally, there is a difference in the average RNFL thickness among individuals with myopia.

Alessandro A. Jammal *et al*., [26] showed the same result in their study. The researchers have shown that age plays a crucial role in modifying the association between IOP and the progressive thinning of the RNFL in individuals with glaucoma. Elderly individuals may exhibit a higher vulnerability to the advancement of glaucoma compared to younger individuals with similar in IOP levels. This susceptibility may be attributed to the fact that glaucoma is an optic neuropathy defined by a gradual decline and death of retinal ganglion cells, which diminish in number as individuals age.

Conclusions

The diagnosis of glaucoma with myopia is a controversy due to the alterations in the optic disc. This research used an OCT technology to investigate the impact of axial length and refractive error on RNFL thickness. The findings revealed that changes in axial length had a differential effect, with the exception of the temporal quadrant. The presence or severity of changes in the temporal quadrant is often minimal or non-existent. The thinning in the temporal quadrant may indicate the glaucoma

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