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ORIGINAL ARTICLE

Evaluation of the Ganglion Cell Layer Complex Thickness by Optical Coherence Tomography in Children with Different Refractive Status

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Abstract

Background: ***Optical Coherence Tomography (OCT) is a non-contact, non-invasive technique that detects the echo magnitude time delay time of backscattered light via low-coherence interferometry.***

Aim: ***To investigate and compare ganglion cell layer thickness between children with refractive error (myopia and hyperopia), helping later-on earlier detection of disorders that possess damaging effects on such layers as glaucoma.***

Patients and methods: ***This cross-sectional observational research was performed on 240 of 120 children attending Al-Azher University hospitals and Port Said Ophthalmology Hospital, Egypt. They were separated into three collections: Group I Involved 80 eyes of children with axial myopia, Group II Involved 80 eyes of children with hyperopia, and Group III Involved 80 eyes of children with emmetropes.***

Results: ***Axial length was highest among the myopic group, 24.15±0.25, than the emmetropic group (22.92±0.33) and hyperopic group (21.8±0.30) with a statistically significant difference ($p<0.001$). The superior, inferior, and total ganglion cell complex (GCC) layers were thinner among the myopic group than the emmetropic group and hyperopic collection with statistically significant variance ($p<0.001$). All GCC showed insignificant correlations with age in all collections. There is a significant direct correlation between axial length with (superior GCC, inferior GCC, and total average GCC measurements) in all groups.***

Conclusion: ***There is no discernible correlation between retinal thinning in isolation & the refractive outcome or visual function of individuals., with some studies indicating no relationship between SE and GCC, while others have contradictory findings.***

Keywords: GCC; Myopia; Hyperopia; Glaucoma

1. Introduction

Refractive errors are prevalent during childhood, and according to the World Health Organization, 153 million individuals globally suffer from visual impairment as a result of uncorrected refractive errors. Myopia has emerged as a significant public health concern, particularly in Asia, where its incidence and severity have reached epidemic proportions.[1]

In Egypt, Gawdat et al., in 1976, showed that myopia has a prevalence of 7.4%.[2] (while in 2015, Massoud and Nassr estimated that about 10.8% of university students are myopic, suggesting that the prevalence of myopia among Egyptians has risen steadily over time.[3]

Optical Coherence Tomography is a non-contact and non-invasive technique that utilizes low-coherence interferometry to determine the time delay and echo magnitude of backscattered light that is reflected from a target object. This enables the investigation of the microstructure present within turbid media. OCT is comparable to the US, with the exception that light is utilized rather than sound, and optical waves are measured as opposed to acoustic or radio waves, hence the term (optical). Additionally, OCT can produce a cross-sectional image of the anterior eye and retina, hence the name tomography.[4]

Spectral-domain optical coherence tomography (SD-OCT) is capable of evaluating retinal layers, such as the inner plexiform layer and macular ganglion cell layer, in addition to the peripapillary retinal nerve fiber layer and macular Thickness, due to its enhanced resolution.[5]

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Ganglion cells are the initial cells to be impacted in cases of glaucoma, with the parafoveal region housing roughly fifty percent of these cells.[6]

In glaucoma individuals, optical coherence tomography has been utilized extensively to assess structural integrity. Assessing the Thickness of the interior plexiform layer (GCIPL) of ganglion cells in POAG.[7]

Despite the generally low occurrence of glaucoma at this stage of life, investigating the normal Thickness of the retinal ganglion cell layer, which may serve as a benchmark in children and adolescents suspected of having glaucomatous nerve fiber faults, continues to be a fascinating area of study. Determining the normal range of retinal ganglion cell layer thickness as determined by OCT is therefore necessary in order to develop a method for early detection of glaucoma in children and adolescents.[8]

This study aimed to investigate and compare ganglion cell layer thickness between children with refractive error (myopia and hyperopia), helping later on in the detection of disorders that possess damaging effects on such layers as glaucoma.

2. Patients and methods

This cross-sectional observational research was performed on 240 of 120 children attending Al-Azher university hospitals and Port Said Ophthalmology Hospital, Egypt divided into three collections: Group I: Involved 80 eyes of children with axial myopia, Group II: Included 80 eyes of children with hyperopia and Group III: Included 80 eyes of children with emmetropel.

Inclusion criteria: By history and examination: Age between 6 and 16 years old, both sexes, emmetropic children with spherical equivalent between +1 and -1 diopter, myopic children with spherical equivalent between (-1 and - 6 diopter) and hyperopic children with spherical equivalent between (+1 and +6 diopter).

Exclusion criteria: By history and examination: Children who are uncooperative, children who have squint, amblyopia, otherwise hyperopia of six diopters otherwise more, lid abnormalities that interfere with imaging, corneal infection, corneal scars, congenital congenital nystagmus, juvenile glaucoma, congenital cataract, illnesses of the optic nerve or retina, & mental illness are all examples of conditions that pose a challenge for medical professionals.

Sample size

The sample size was calculated utilizing the following formula:[9]

$$n = 2\left[\frac{\left(Z_{\alpha/2} + Z_{\beta}\right) * \sigma}{\mu_1 - \mu_2}\right]^2$$

Where:

n = sample size

$Z\alpha/2$ = 1.96 (The critical value that divides the central 95% of the Z distribution from the 5% in the tail)

$Z\beta$ = 0.84 (The critical value that separates the lower 20% of the Z distribution from the upper 80%)

σ = the estimate of the standard deviation of GCC thickness = 6.29 μm [10]

$\mu 1$ = mean in the myopic group = 82.59 μm[10]

$\mu 2$ = mean in the emmetropic group = 77.17 μm [10]

So, by calculation, the sample size was 240 eyes, which were subdivided into three groups.

Sampling method: Convenience sampling of all myopic, emmetropic, and hyperopic children attending Al-Azher University hospitals and Port Said Ophthalmology Hospital, Egypt.

Methodology

All the study participants were subjected to:

Ophthalmic examination: Objective refraction using Autorefractometer (Topcon KR-8900;) calculating post cycloplegic spherical equivalent, followed by the valuation of best corrected distant visual acuity utilizing Landolt C chart was done. Children underwent fundus examination using a binocular indirect ophthalmoscope (Model AAIO-7 Appasamy Associates 2014, India) and Volk double aspheric +20.00D lens (Volk Optical, Ohio 1988) after instillation of cyclopentolate 1.0%, two times with 10 minutes interval, 30 minutes before the examination to exclude any post segment disorders. Examination of ocular motility was conducted, followed by a complete ocular examination using a slit lamp (SL-D7 slit-lamp Topcon Co, Tokyo, Japan) was carried out to exclude any anterior media opacity and examine the anterior segment (e.g., Corneal opacities, dense cataract, and anterior uveitis). The axial length of the globe was measured using A-scan (Sonomed E-Z scan AB5500+, Sonomed Escalon©, New York, USA) after instillation of topical anesthetic eye drops; Benoxinate hydrochloride 0.4% solution (Benox, property of EIPICO 2005, Egypt). Children were divided into three comparison groups: Group A included all emmetropic children with spherical equivalent between (-1 and +1) diopters, whereas Group B involved all myopic children with spherical equivalent between (-1 and - 6) diopters. Group C involves all hyperopic children with a spherical equivalent between (+1 and 6) diopter.

Specific examination: All children were dilated with cycloplegic eye drops (1% cyclopentolate eye drops) before examination. The child's information was entered into the device, including the child's name, gender, race, birth date, identity number, and globe axial length in mm. The measurement of GCC layer thickness was evaluated using OCT (Optical Coherence Tomography 3D OCT-1 MAESTRO). Two scans were acquired, a 3D macular scan and a 3D disc scan; the former includes a point-to-point tomographic analysis of a macular area consisting of 512 horizontal and 256 vertical lines over an area of 7mm x 7mm which yield multiple thickness maps of not only the macula, but also its RNFL, combined ganglion cell/inner plexiform layer thickness (GCIP expressed as GCL+), & combined macular RNFL /GCIP thickness expressed as (GCL++). All of the photos were examined, and the only ones that were considered for inclusion in the research were those that had low movement artifacts and a high signal quality, expressed by the device's automated signal strength analysis in greenish box ≥40. GCL+ (combined Thickness of ganglion cell /inner plexiform layers) was measured at the macular region on SS-OCT images using a specific automatic segmentation algorithm. The overall average of macular GCIP, in addition to the detailed superior and inferior Thickness of macular GCIP, was measured. The measured values among all participants were averaged, generating average GCC thickness values in group A of the emmetropic children, group B of the myopic children, and group C of the hyperopic children in preparation for later statistical analysis.

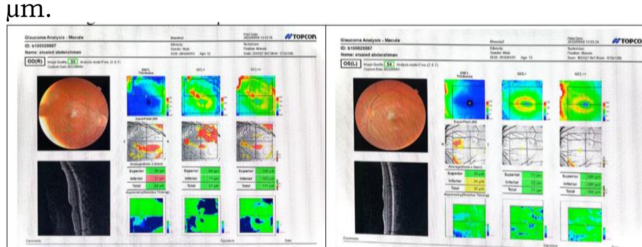
Ethical consideration: The research was reviewed by the ethical committee of the Faculty of Medicine, Al-Azhar University, on February 16th, 2023, to ensure compliance with the study procedures and the ethical guidelines. Informed written consent was obtained from all the participants' parents, and an additional assent was taken from participants between ages 6 and 16 before getting them involved in the study; those who refused participation were not asked to give a reason with no implications upon the provided medical service. The procedures performed in the present study have no harmful effects or are not threatening to children's lives. Participants were informed about all results of procedures and tests performed, either normal or abnormal, and had the right to withdraw. Information confidentiality was kept. Each child was offered the proper management accordingly.

Statistical analysis: Input data into a Microsoft Excel 2010 spreadsheet of the Microsoft Office bundle of Microsoft Corporation, USA, then analyse it utilizing SPSS version 23 (Statistical Package for Social Sciences) of IBM Corporation, USA. Data normality was checked using the Kolmogorov Smirnov test. The quantitative information was presented as the mean value ± standard deviation (SD). The presentation of qualitative data comprised frequency and percentage figures. As needed, various types of charts were employed to visually represent data and establish relationships. The significance of the variation among the two collections was determined utilizing the chi-square test for qualitative data and the independent samples t-test for quantitative data. In order to ascertain the relationships among various variables, the Pearson correlation coefficient (r and ρ) was applied as follows: Weak correlation denotes the range of 0.0-0.3, moderate correlation 0.4-0.6, and strong correlation 0.7-1.0. For statistical significance, a p-value of less than 0.05 was considered (p-value < 0.05).

Examples of OCT disc and macular imaging:

Case 1

A 12 years-old emmetropic male child, A 3D-disc OCT scan was done on both eyes and showed: right eye Sup GCL Thickness = 63 µm, Inf GCL Thickness = 71 µm, total average Thickness is 67 µm. Left eye Sup GCL Thickness = 71 µm, Inf GCL Thickness = 72 µm, total average Thickness is 73 µm.

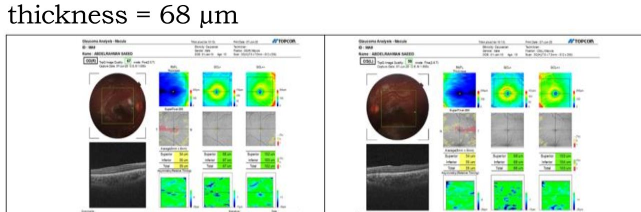


(A): Right eye 3D-Macular OCT imaging of a 12-year-old emmetropic child.

(B): Left eye 3D-Macular OCT imaging of the same 12-year-old child.

Figure 1. Photos of case 1

Case 2: A 10-year-old emmetropic male child, A 3D-disc OCT scan was done on both eyes and showed: Rt eye Sup GCL+ thickness = 68 µm, inf thickness =67 µm and total average GCL+ thickness 67 µm. Lt eye Sup GCL+ thickness = 69 µm, inf thickness = 68 µm and total average thickness = 68 µm



(A): Right eye 3D-Macular OCT imaging of a 10-year-old child.

(B): Left eye 3D-Macular OCT imaging of the same 10-year-old child.

Figure 2. Photos of case 2

3. Results

Age, gender and side of affection were comparable between groups with statistical insignificant difference (p<0.05) (Table 1).

Table 1. Demographic data among research groups.

	MYOPIC GROUP (N=80)	HYPEROPIC GROUP (N=80)	EMMETROPIC GROUP (N=80)	TEST VALUE	P-VALUE	SIG.
AGE (YEARS) MEAN±SD	11.4±2.1	11.3±2.2	11.6±2.8	0.288	0.782[1]	NS
GENDER (N, %)				1.438	0.487[2]	NS
MALE	38(47.5%)	44(55%)	46(56.8%)			
FEMALE	42(52.5%)	36(45%)	34(43.2%)			
SIDE OF PRESENTATION (N, %)				0.00	1.00[2]	NS
RIGHT EYE	40(50%)	40(50%)	40(50%)			
LEFT EYE	40(50%)	40(50%)	40(50%)			

ANOVA test, Chi-square test used, *Significant when p<0.05

Axial length was highest among myopic group 24.15±0.25 than emmetropic group (22.92±0.33) and hyperopic group (21.8±0.30) with statistically significant variance (p<0.001) (Table 2).

Table 2. In contrast between study groups in Axial-scan results.

	MYOPIC GROUP (N=80)	HYPEROPIC GROUP (N=80)	EMMETROPIC GROUP (N=80)	TEST VALUE	P-VALUE	SIG.
AXIAL LENGTH MEAN±SD	24.15±0.25*	21.8±0.30*	22.9±0.33*	124.1	<0.001*[1]	S

ANOVA t test, Post hoc test, *Significant when p<0.05, IOP; intraocular pressure.

Superior, inferior and total GCC layer was thinner among myopic group than emmetropic group and hyperopic group with statistically significant variance (p<0.001) (Table 3).

Table 3. In contrast amongst study groups in thickness of ganglion cell complex.

	MYOPIC GROUP (N=80)	HYPEROPIC GROUP (N=80)	EMMETROPIC GROUP (N=80)	TEST VALUE	P-VALUE	SIG.
SUPERIOR GCC (UM) MEAN±SD	65.8±2.3	73.9±1.9	69.9±2.0	295.8	<0.001*[1]	S
INFERIOR GCC (UM) MEAN±SD	65.6±1.9	73.5±1.7	70.4±1.4	440.2	0.002*[1]	S
TOTAL GCC (UM) MEAN±SD	65.9±1.9	73.8±1.9	70.2±1.7	370.4	<0.001*[1]	S

Independent t test, *Significant when p<0.05, GCC = Ganglion Cell Complex

All GCC showed insignificant correlations with age in all groups (Table 4).

Table 4. Correlations of GCC with Age.

		Age		
		Myopic group (n=80)	Hyperopic group (n=80)	Emmetropic group (n=80)
Superior ganglion cell complex thickness (um)	R	0.068	-0.178	-0.177
	p-value	0 .550	0.115	0.115
Inferior ganglion cell complex thickness (um)	R	0.164	-0.155	-0.161
	p-value	0.196	0.169	0.154
Average ganglion cell complex thickness (um)	R	0.093	-0.126	-0.185
	p-value	0.412	0.256	0.099

Was noted a significant direct correlation amongst axial length with (superior GCC, inferior GCC and total average GCC measurements) in all groups (Table 5).

Table 5. Correlation between axial length and the study variables

		Axial length		
		Myopic group (n=80)	Hyperopic group (n=80)	Emmetropic group (n=80)
Superior ganglion cell complex thickness (um)	R	0.579**	0.208	0.642**
	p-value	<0.001	0.064	<0.001
Inferior ganglion cell	R	0.488**	0.222*	0.574**

complex thickness (um)	p-value	<0.001	0.048	<0.001
Average ganglion cell	R	0.580**	0.303*	0.598**
complex thickness (um)	p-value	<0.001	0.006	<0.001

4. Discussion

The functional correlation between decreased spatial resolution and a diminished thickness of the middle to inner retina has been identified as the underlying cause of retinal thinning in myopia. As occurs in pathologic myopia, this thinning has been attributed to the straining of the ocular layers during eyeball elongation. Additionally, elevated axial length has been linked to constricted retinal arterioles and reduced peripapillary retinal flow perfusion; however, it remains debatable whether this vascular compromise occurs prior to or subsequent to the thinning of the RNFL.[11]

In our study, the myopic group had significantly lower ganglion cell complex Thickness than the emmetropic group, the hyperopic with p<0.001.

In a similar vein, a cross-sectional investigation scrutinized the eyes of thirty-two individuals with unilateral amblyopic conditions. Spectral-domain OCTA was utilized to evaluate factors including GCC thickness, macular Thickness (comprising the inner, total, and outer layers), and VD in the macular and optic nerve regions. The Thickness of ganglion cell complexes in various macular areas was considerably reduced in amblyopic eyes relative to their sighted peers.[12]

This is with respect to the Altimer et al. [13] research, which found that the ganglion cell layer thickness of myopic participants was lower than in emmetropic participants. This finding aligns with previous investigations performed in adult populations.[14]

Inconsistent with the results reported in prior research [15,16] Our research revealed a positive correlation between GCC thickness and AL. Additionally, we discovered that hyperopic children had thicker GCC, involving superior and inferior GCC, than myopic children (P0.0001). Nonetheless, multiple investigations have failed to establish a correlation between AL and GCC thickness.[17] This could potentially be attributed to the age disparity between the participants (adults versus infants), suggesting that age may have an influence on the outcomes. Histopathological studies have demonstrated in the past that myopia develops in response to an increase in AL and ocular expansion. Elongation of the ocular may induce mechanical stretching and traction, both of which may contribute to the thinning of the retina and sclera in individuals with myopia.[18]

This is similar to the results of another investigation, which discovered that the nasal, superior, inferior, and average RNFL thicknesses of myopic eyes were considerably reduced in comparison to those of normal eyes. Significantly higher average, superior, and inferior ganglion cell complex values were observed in eyes with low to moderate myopia compared to eyes with high myopia.[19]

A recent systematic review and meta-analysis incorporated findings from forty-seven investigations involving a combined total of 12223 eyes, of which 8600 were instances, and 3623 were non-cases. The findings indicated that highly myopic eyes exhibited substantially reduced values for macular GCC, mean macular Thickness, parafoveal, perifoveal, macular GC-IPL, foveolar, foveal, RNFL, and pRNFL Thickness when compared to the control group. Moderately myopic eyes exhibited a considerably reduced mean macular GCC layer and pRNFL in comparison to the control group. The results of the research validate the distinctions in retinal OCT assessments among eyes with myopia and hyperopia in comparison to the control group, underscoring the potential biomarker value of OCT measurements for ocular pathologies.[20]

Age did not correlate significantly with GCC thickness, which is consistent with the findings of a number of prior studies.[16] On the contrary, a number of studies have found that the Thickness of the retina decreases as age increases in adults.[21, 22]

This inconsistency may be attributed to the fact that our participants were young infants. Future longitudinal research examining the relationship between GCC thickness and age would be beneficial.

Our research was not without limitations. No longitudinal follow-up was conducted to compare the three collections in terms of the rate of GCC thickness.

Recommendations:

In brief, the results of the present investigation validate the distinctions in OCT measurements among myopic and hyperopic eyes relative to the control group, with a particular focus on glaucoma. These results underscore the benefits of assessing OCT measurements as prospective biomarkers of ocular pathologies caused by severe refractive errors. Moreover, the potential correlation between refractive errors and OCT assessments of retinal layers may suggest the need to reassess the previously established standard. In the future, similar measurements in similar cohorts will be repeated in order to obtain longitudinal data, which will be needed to establish reference database values for GCC layer thickness in such age groups.

4. Conclusion

There was no observed correlation between retinal thinning in isolation and the refractive result or visual function of the individuals. Prior research has examined the correlation between retinal Thickness and refractive status; some investigations have concluded that SE and GCC are unrelated, whereas others have demonstrated the exact opposite.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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