

## Age-Related Changes in Retinal Nerve Fiber Layer and Ganglion Cell Complex Measured with Optical Coherence Tomography

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### Abstract

**Background:** Age-related changes in ocular structures and function are of strong interest in knowing the impact of aging on visual health. Optical Coherence Tomography (OCT) has proven to be a valuable tool in assessing retinal nerve fiber layer (RNFL) thickness and macular ganglion cell complex (GCC), as indicators of retinal health. **This study aimed to** study age-associated change in peripapillary RNFL thickness and macular ganglion cell complex, in healthy participants, measured with the SD-OCT device. **Methods:** This prospective observational cross-sectional and analytical research- was performed on eighty patients; divided into 4 groups (twenty eyes in each group) with age range 20-29, 30-39, 40-49 and 50-59 years old. All cases underwent demographic and full ophthalmic investigation. **Results:** The results revealed considerable changes in and age terms, with females showing a significantly higher prevalence in the studied groups. Considerably higher ages were detected in Group IV than the other three groups, in Group III than in both Group II and I, and in Group II than Group I. Regarding retinal parameters, the study noticed significantly different in temporal RNFL thickness among Group I and IV (P-value < 0.05) also, between Group II and IV (P-value < 0.05). **Conclusions:** RNFL thickness of healthy subjects was associated with age, particularly in the temporal areas. There was no considerable change between the groups investigated as regard; superior macular RNFL, inferior macular RNFL, and total macular RNFL. Age-associated RNFLT in healthy participants- assessed using OCT- does not detect the same slope in every sector/quadrant.

**Keywords:** Age-Related Changes; RNFL; Ganglion Cell Complex; OCT; Peripapillary RNFL Thickness.

## Introduction

The retina is a complex and intricate neural tissue located at the back of the eye. It plays an essential part in vision by transforming light into electrical impulses that the brain can comprehend. Retinal Nerve Fibre Layer (RNFL) and Ganglion Cell Complex (GCC) are two essential retinal structures that have received considerable interest in ophthalmic research<sup>[1]</sup>. The RNFL is composed up of axons from retinal ganglion cells., which transmitting visual data to the brain. The GCC comprises the ganglion cell, inner nuclear layers and inner plexiform. Together, the RNFL and GCC are vital for maintaining visual function and integrity<sup>[2]</sup>.

Aging is a natural process that affects various tissues and organs in the human body, including the eye. The retina is not exempt from age-related changes, and understanding these alterations is of great clinical importance<sup>[3]</sup>. Optical coherence tomography (OCT) has reformed ophthalmic imaging by providing the retina cross-sectional scans and high-resolution. It permits accurate measurements of RNFL thickness, and GCC integrity, enabling clinicians and researchers to assess age-related variations in these retinal layers<sup>[4]</sup>.

Numerous studies have investigated age-related changes in the RNFL and GCC using OCT in both healthy individuals and those with ocular diseases. These investigations have revealed that aging is related to RNFL and GCC thinning<sup>[5, 6]</sup>. The exact

mechanisms underlying these changes are not fully understood but may involve factors such as reduced cellular density, decreased axonal transport, and alterations in retinal blood supply. Elucidating the age-associated variations in GCC and RNFL- is crucial for distinguishing normal aging from pathological conditions and for identifying individuals at risk for age-related eye diseases<sup>[7]</sup>.

Previous research has demonstrated that age-associated changes in GCC and RNFL are not uniform across the retina. Different regions of the retina may exhibit varying degrees of thinning or structural alterations<sup>[5]</sup>. The peripapillary region, which surrounds the optic nerve head, is commonly examined for assessing RNFL thickness, while the macular region is frequently evaluated for GCC measurements. By investigating both regions, a comprehensive understanding of age-related changes in the retina could be achieved<sup>[8]</sup>.

Moreover, several factors may influence the age-associated changes observed in GCC and RNFL. These factors include gender, ethnicity, refractive error, systemic conditions (e.g., hypertension, diabetes), and environmental factors (e.g., smoking, sunlight exposure). Considering these potential confounding variables is essential when interpreting age-related alterations in the retinal layers<sup>[9]</sup>.

This research intended to investigate the age-related changes in peripapillary

RNFL thickness and macular GCC, assessed with the SD-OCT device, in healthy participants.

## Methods

This prospective cross-sectional trial was performed at the Ophthalmology Department of Benha University Hospital. The research aimed to investigate a specific population and included eighty patients divided into four groups, each consisting of twenty eyes. The age ranges of the groups were 20-29, 30-39, 40-49, and 50-59 years old. This study extended from May 2022 to December 2022. All procedures are approved by local Research Ethical Committee of Benha Faculty of Medicine. **Research ethics committee: Ms.8.3.2020**

**Inclusion criteria** were participants aged between 20 and 59 years, irrespective of gender, with errors of refraction and anisometropia of at least +1.0D (spherical equivalent). The participants were required to have a normal fundus and optic disc size between 2-3mm, axial length was 22 to 24.5 mm, and intraocular pressure (IOP) quantified by applanation tonometry below 22mm Hg without any anti-glaucoma medication. Additionally, they should not have a history of previous eye diseases, trauma, eye surgery, systemic diseases affecting the disc and macula, or contraindications for pupil dilatation.

**On the other hand, The exclusion criteria** were patients with previous intraocular surgery or ocular injuries, as well as those with strabismus,

amblyopia, glaucoma, optic nerve cup disc ratio  $> 0.5$  or asymmetry exceeding 0.2 between the two eyes, retinal pathology, or prematurity, metabolic, neurologic, other systemic diseases. Additionally, individuals with media opacity that hindered OCT acquisition with good signal strength, OCT scan signal strength below 5/10, contraindication of pupil dilatation, or dry eye- were also excluded. These exclusion criteria were implemented to ensure that the study population consisted of individuals without any confounding factors that could potentially impact the study outcomes.

The operational design: Firstly, each participant's informed consent was obtained. Then, various demographic data were obtained, including age, gender, previous intraocular surgery, and presence of neurologic, metabolic, or systemic disorders. Co-morbidities such as; diabetes, hypertension, cardiac, hepatic, or renal pathology- were also recorded.

Ophthalmologic investigations were conducted, like valuation of best corrected visual acuity (BCVA) utilizing a tumbling E eye chart, IOP assessment by Goldman Applanation Tonometer, slit lamp Biomicroscopy for anterior segment evaluation, evaluation of the pupil for relative afferent pupillary defect (RAPD) before pupil dilation, cycloplegic autorefractometry assessment, and posterior segment evaluation by indirect ophthalmoscope and slit lamp Biomicroscopy following pupil dilation. OCT was performed to assess circumpapillary retinal nerve fiber layer

(cpRNFL) and GCC thickness by SD-OCT technology.

Regarding the time schedule of the study, the preparatory phase lasted for one month, the design of the examination sheet took two months, the literature review was conducted for three months, and the collection, organization, data entry, and statistical analysis required four months.

### Statistical analysis:

The study's data were analysed using version 20.0 of the IBM SPSS software suite (Armonk, NY: IBM Corp). The Chi-square test was used to compare qualitative data provided as numbers and proportions. Using the Shapiro-Wilk test, the normality of the distribution of quantitative data was determined. The interquartile range, range, mean, standard deviation, and median were utilised to identify the numerical variable. The significance of the findings was determined using a 5% significance threshold. The F-test (ANOVA)- was used to compare several groups with quantitative variables that were normally distributed, followed by the Post Hoc test (Tukey) for pairwise comparisons. When working with quantitative data whose distribution is abnormal, The Kruskal-Wallis test was used to compare more than two groups.

### Results

A substantially considerable change was seen among studied groups as regard age, as group IV exhibited a significantly increased age than the remaining three groups. Similarly,

group III had a significant higher age than group I and II. Furthermore, group II demonstrated a higher age in comparison to group I ( $P < 0.001$ ), **Table (1)**.

The research found a significant variation in IOP between the groups that were examined ( $P = 0.032$ ). Specifically, group II had a significant increased IOP than group IV ( $P = 0.002$ ), while the IOP levels were not significant different among the other groups, **Table (1)**.

There were significantly difference observed in axial length within the investigated groups ( $P = 0.001$ ). Specifically, group II had a significant increased axial length than group I ( $P = 0.025$ ), and group IV had a significant increased axial length than group I ( $P < 0.001$ ). However, the differences in axial length among the other studied groups were not statistically significant. Regarding optic disc size, there were significantly different observed within the investigated groups ( $P < 0.001$ ). Group II had a significantly lower optic disc size compared to group I ( $P < 0.001$ ), and it was also significant decreased in group II than both group III and IV ( $P < 0.001$ ). However, there were not significantly different in optic disc size among the other studied groups. The cup-to-disc ratio (C/D ratio) did not show any significantly different among the studied groups, **Table (1)**.

The LogMAR values for the studied groups were as follows: group I had a mean  $\pm$  SD of  $0.0 \pm 0.0$ , group II had  $0.05 \pm 0.05$ , group III had  $0.08 \pm 0.07$ ,

and group IV had  $0.2 \pm 0.0$ . The analysis revealed a significantly different in LogMAR within the investigated groups ( $P < 0.001$ ). Specifically, LogMAR was lower in group I than the other groups ( $P = 0.036, 0.003, <0.001$ , respectively). Additionally, LogMAR was significant decreased in groups II and III than group IV ( $P < 0.001$ ). However, there was not significantly different detected between groups II and III, **Table (2)**.

The cpRNFL thickness (inferior, superior, nasal, and total thickness) exhibited insignificant different among the studied groups. Temporal thickness was significantly increase in group I than group IV ( $P < 0.016$ ). Moreover, both group II and III exhibited significantly higher temporal thickness than group IV ( $P < 0.001$  and  $0.047$ , respectively), **Table (3)**.

In terms of superior macular RNFL, inferior macular RNFL, and total macular RNFL, no statistically significant differences were identified between the analysed groups, **Table (4)**.

The mean  $\pm$  SD of superior Macular RNFL was  $34.45 \pm 5.91$  in group I,  $32.40 \pm 2.68$  in group II,  $32.80 \pm 3.16$  in group III, and was  $34.50 \pm 2.86$  in group IV. The mean  $\pm$  SD of Inferior Macular RNFL was  $34.60 \pm 5.20$  in group I,  $32.15 \pm 2.89$  in group II,  $34.70 \pm 3.08$  in group III, and was  $34.05 \pm 3.47$  in group IV. The mean  $\pm$  SD of Total Macular RNFL was  $34.35 \pm 5.32$  in group I,  $32.25 \pm 1.89$  in group II,  $33.65 \pm 3.22$  in group III, and was  $34.30 \pm 2.90$  in group IV. There was an insignificant difference among the studied groups as regard (superior macular RNFL, inferior macular RNFL, and total macular RNFL), **Table (5)**.

**Table (6)** shows comparison between the different studied groups according to ganglion cell layer (Gcl). shows comparison between the different studied groups according to inner plexiform layer (Gcl). A substantial inverse association existed between LogMAR and temporal circumpapillary RNFLT ( $r = -0.305$ ,  $P \text{ value} = 0.006$ ).

**Table (1):** Comparison between the different studied groups according to demographic data, Comparison between the different studied groups according to IOP by Applanation

Demographic Data	Group I (n=20)		Group II (n=20)		Group III (n=20)		Group IV (n=20)		p
	No.	%	No.	%	No.	%	No.	%	
<b>Sex</b>									
<b>Male</b>	0	0.0	10	50.0	8	40.0	3	15.0	0.001*
<b>Female</b>	20	100.0	10	50.0	12	60.0	17	85.0	
<b>Age (years)</b>									
<b>Min. – Max.</b>	21.0 – 26.0		34.0 – 38.0		40.0 – 49.0		50.0 – 60.0		<0.001*
<b>Mean ± SD.</b>	23.60 ± 1.96		36.20 ± 1.44		45.20 ± 2.67		55.45 ± 3.24		
<b>Median (IQR)</b>	24.0 (22.0–26.0)		36.0 (36.0–38.0)		45.50 (43.0–47.0)		56.0 (55.0–57.0)		
<b>Sig. bet. groups</b>	p <sub>1</sub> <0.001*, p <sub>2</sub> <0.001*, p <sub>3</sub> <0.001*, p <sub>4</sub> <0.001*, p <sub>5</sub> <0.001*, p <sub>6</sub> <0.001*								
<b>IOP by Applanation (mmHg)</b>	Group I (n=20)	Group II (n=20)	Group III (n=20)	Group IV (n=20)	F	p			
<b>Min. – Max.</b>	13.0 – 18.0	13.0 – 20.0	12.0 – 19.0	13.0 – 17.0	3.082*	0.032*			
<b>Mean ± SD.</b>	15.55 ± 1.43	16.70 ± 2.20	16.0 ± 1.81	15.0 ± 1.81					
<b>Median (IQR)</b>	16.0 (15.0–16.0)	17.0 (15.0–18.0)	16.0 (15.0–17.0)	15.0 (13.0–17.0)					
<b>Sig. bet. grps</b>	p <sub>1</sub> =0.203, p <sub>2</sub> =0.865, p <sub>3</sub> =0.778, p <sub>4</sub> =0.624, p <sub>5</sub> =0.022*, p <sub>6</sub> =0.318								

SD: Standard Deviation, IQR - Interquartile Range, IOP: Intraocular Pressure, \*: significant as P-value < 0.05, p<sub>1</sub>: p value for comparing between Group I and Group II, p<sub>2</sub>: p value for comparing between Group I and Group III, p<sub>3</sub>: p value for comparing between Group I and Group IV, p<sub>4</sub>: p value for comparing between Group II and Group III, p<sub>5</sub>: p value for comparing between Group II and Group IV, p<sub>6</sub>: p value for comparing between Group III and Group IV.

**Table (2):** Comparison between the different studied groups according to axial length, optic disc size and C/D ratio

	Group I (n=20)	Group II (n=20)	Group III (n=20)	Group IV (n=20)	Test of sig.	p
<b>Axial length</b>						
<b>Min. – Max.</b>	22.78 – 23.39	22.85 – 23.70	22.70 – 24.20	22.85 – 24.02	F= 6.199*	0.001*
<b>Mean ± SD.</b>	23.01 ± 0.22	23.36 ± 0.28	23.31 ± 0.48	23.52 ± 0.47		
<b>Median (IQR)</b>	23.0 (22.78 – 23.10)	23.42 (23.32 – 23.52)	23.19 (22.84 – 23.80)	23.82 (22.93 – 23.87)		
<b>Sig. bet. Groups</b>	p <sub>1</sub> =0.025*, p <sub>2</sub> =0.080, p <sub>3</sub> <0.001*, p <sub>4</sub> =0.967, p <sub>5</sub> =0.554, p <sub>6</sub> =0.289					
<b>Optic disc size</b>						
<b>Min. – Max.</b>	2.55 – 3.0	2.03 – 2.80	2.19 – 2.97	2.51 – 2.92	F= 18.012*	<0.001*
<b>Mean ± SD.</b>	2.85 ± 0.14	2.41 ± 0.23	2.69 ± 0.23	2.74 ± 0.17		
<b>Median (IQR)</b>	2.91 (2.83 – 2.94)	2.44 (2.17 – 2.55)	2.81 (2.51 – 2.87)	2.83 (2.51 – 2.88)		
<b>Sig. bet. Groups</b>	p <sub>1</sub> <0.001*, p <sub>2</sub> =0.059, p <sub>3</sub> =0.271, p <sub>4</sub> <0.001*, p <sub>5</sub> <0.001*, p <sub>6</sub> =0.881					
<b>C/D ratio</b>						
<b>Min. – Max.</b>	0.15 – 0.45	0.18 – 0.50	0.10 – 0.45	0.13 – 0.48	H= 1.787	0.618
<b>Mean ± SD.</b>	0.29 ± 0.10	0.31 ± 0.11	0.29 ± 0.10	0.28 ± 0.14		
<b>Median (IQR)</b>	0.27 (0.19 – 0.41)	0.27 (0.21 – 0.40)	0.32 (0.21 – 0.35)	0.26 (0.15 – 0.40)		

C/D ratio: Cup-to-Disc Ratio, SD: Standard Deviation, IOP: Intraocular Pressure, \*: significant as P-value < 0.05, p<sub>1</sub>: p value for comparing between Group I and Group II, p<sub>2</sub>: p value for comparing between Group I and Group III, p<sub>3</sub>: p value for comparing between Group I and Group IV, p<sub>4</sub>: p value for comparing between Group II and Group III, p<sub>5</sub>: p value for comparing between Group II and Group IV, p<sub>6</sub>: p value for comparing between Group III and Group IV.

**Table (3):** Comparison between the different studied groups according to LogMAR

	Group I (n=20)	Group II (n=20)	Group III (n=20)	Group IV (n=20)	Test sig.	of p
<b>LogMAR</b>						
<b>Min. – Max.</b>	0.0 – 0.0	0.0 – 0.1	0.0 – 0.2	0.2 – 0.2	H=	<0.001*
<b>Mean ± SD.</b>	0.0 ± 0.0	0.05 ± 0.05	0.08 ± 0.07	0.2 ± 0.0	56.234*	
<b>Median (IQR)</b>	0.0 (0.0 – 0.0)	0.05 (0.0 – 0.1)	0.1 (0.0 – 0.1)	0.2 (0.2 – 0.2)		
<b>Sig. bet. Groups</b>	p1=0.036*, p2=0.003*, p3<0.001*, p4=0.377, p5<0.001*, p6<0.001*					

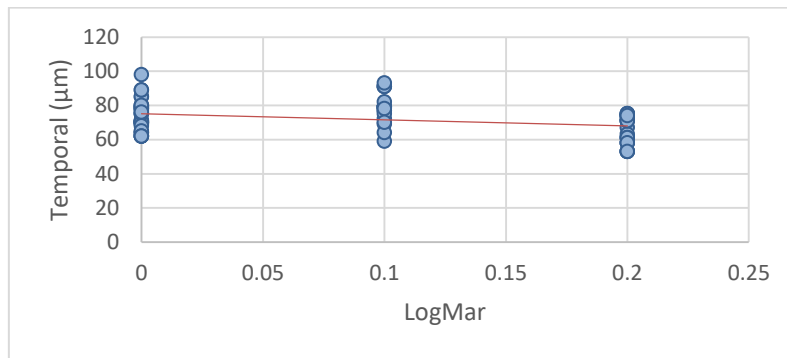
LogMAR - Logarithm of the Minimum Angle of Resolution, SD: Standard Deviation, \*: significant as P-value < 0.05, p1: p value for comparing between Group I and Group II, p2: p value for comparing between Group I and Group III, p3: p value for comparing between Group I and Group IV, p4: p value for comparing between Group II and Group III, p5: p value for comparing between Group II and Group IV, p6: p value for comparing between Group III and Group IV.

**Table (4):** Comparison between the different studied groups according to circum-papillary retinal nerve fibre layer thickness

circumpapillary retinal nerve fiber layer thickness	Group I (n=20)	Group II (n=20)	Group III (n=20)	Group IV (n=20)	F	p
<b>Superior</b>						
<b>Min. – Max.</b>	107.0 – 147.0	100.0 – 138.0	97.0 – 152.0	109.0 – 141.0	1.960	0.127
<b>Mean ± SD.</b>	128.05 ± 11.72	122.85 ± 12.37	118.05 ± 16.76	124.20 ± 11.16		
<b>Median (IQR)</b>	126 (124–138)	124 (117–134)	114.5 (103.5–132.5)	119.0 (119 – 136)		
<b>Inferior</b>						
<b>Min. – Max.</b>	118.0 – 140.0	126.0 – 138.0	104.0 – 137.0	119.0 – 140.0	4.231	0.008*
<b>Mean ± SD.</b>	129.90 ± 9.90	132.60 ± 3.45	123.80 ± 8.0	129.05 ± 9.09	*	
<b>Median (IQR)</b>	132.0 (119–139)	133 (131.5–134.5)	124.5 (121–128.5)	127.50 (120–139)		
<b>Sig. bet. groups</b>	p1=0.711, p2=0.084, p3=0.987, p4=0.005*, p5=0.502, p6=0.171					
<b>Nasal</b>						
<b>Min. – Max.</b>	62.0 – 97.0	59.0 – 93.0	66.0 – 114.0	68.0 – 102.0	1.354	0.263
<b>Mean ± SD.</b>	78.10 ± 13.10	75.10 ± 10.49	82.35 ± 13.86	81.05 ± 12.0		
<b>Median (IQR)</b>	71.0 (69.0–92.0)	76.50 (68.0–80.0)	79.50 (72.5–87.0)	84.0 (69.0–88.0)		
<b>Temporal</b>						
<b>Min. – Max.</b>	64.0 – 85.0	62.0 – 91.0	59.0 – 98.0	53.0 – 75.0	6.841	<0.001*
<b>Mean ± SD.</b>	73.75 ± 6.63	77.55 ± 9.39	72.60 ± 10.20	65.15 ± 8.89	*	*
<b>Median (IQR)</b>	71.0 (69.50–79.0)	78.0 (72.50–84.0)	71.0 (64.50–77.50)	66.0 (58.0–74.0)		
<b>Sig. bet. groups</b>	p1=0.532, p2=0.977, p3=0.016*, p4=0.299, p5<0.001*, p6=0.047*					
<b>Total thick</b>						
<b>Min. – Max.</b>	92.0 – 112.0	98.0 – 106.0	86.0 – 115.0	92.0 – 109.0	0.921	0.435
<b>Mean ± SD.</b>	101.0 ± 6.46	102.60 ± 2.70	99.40 ± 8.18	100.25 ± 6.67		
<b>Median (IQR)</b>	100.0 (96.5–105.0)	102.50 (101–105)	100.0 (91.5–107.5)	98.0 (95.0–108.0)		

**Table (5):** Comparison between the different studied groups according to Macular RNFL

Macular RNFL	Group I (n=20)	Group II (n=20)	Group III (n=20)	Group IV (n=20)	F	p
<b>Superior (um)</b>						
<b>Min. – Max.</b>	30.0 – 51.0	29.0 – 38.0	27.0 – 38.0	31.0 – 39.0	1.593	0.198
<b>Mean ± SD.</b>	34.45 ± 5.91	32.40 ± 2.68	32.80 ± 3.16	34.50 ± 2.86		
<b>Median (IQR)</b>	33.0 (31.50-34.50)	32.0 (31.0-34.0)	33.50 (30.0-35.0)	34.0 (32.0-37.0)		
<b>Inferior (um)</b>						
<b>Min. – Max.</b>	29.0 – 48.0	28.0 – 36.0	30.0 – 41.0	29.0 – 39.0	1.975	0.125
<b>Mean ± SD.</b>	34.60 ± 5.20	32.15 ± 2.89	34.70 ± 3.08	34.05 ± 3.47		
<b>Median (IQR)</b>	34.0 (31.0-35.0)	32.0 (30.0-35.0)	34.50 (32.0-37.50)	35.0 (31.0-37.0)		
<b>Total (um)</b>						
<b>Min. – Max.</b>	30.0 – 49.0	29.0 – 35.0	29.0 – 39.0	31.0 – 39.0	1.511	0.218
<b>Mean ± SD.</b>	34.35 ± 5.32	32.25 ± 1.89	33.65 ± 3.22	34.30 ± 2.90		
<b>Median (IQR)</b>	33.0 (31.0-35.0)	32.0 (31.0-35.50)	33.50 (31.0-36.50)	34.0 (32.0-37.0)		



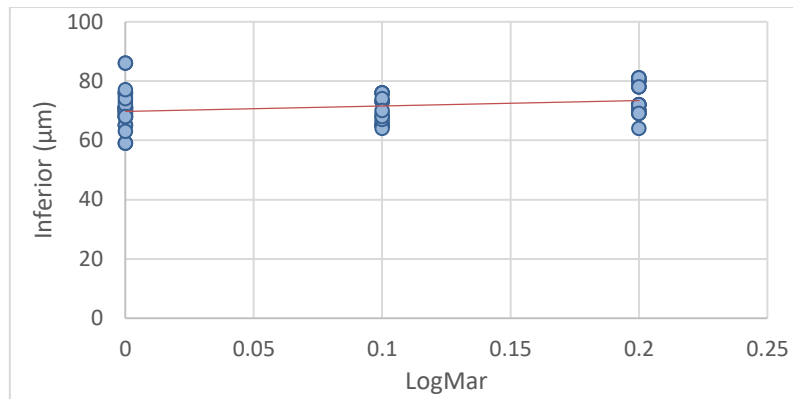
**Fig1:** Correlation between LogMAR and temporal cpRNFL thickness

Significant association exists between LogMAR and inferior ganglion cell layer thickness (r= 0.281, P value=0.012).



**Table (6):** Comparison between the different studied groups according to ganglion cell layer (Gcl)

ganglion cell layer (Gcl)	Group (n=20)	I Group (n=20)	II Group (n=20)	III Group (n=20)	IV Group (n=20)	F	p
<b>Superior (um)</b>							
<b>Min. – Max.</b>	66.0 – 89.0	64.0 – 76.0	63.0 – 79.0	71.0 – 79.0			
<b>Mean ± SD.</b>	74.0 ± 5.80	69.80 ± 4.09	71.25 ± 4.27	74.35 ± 3.22	4.87		0.004*
<b>Median (IQR)</b>	73.0 (71.0–75.0)	69.0 (67.0–74.0)	72.0 (68.0–74.50)	73.0 (72.0–78.0)	7*		
<b>Sig. bet. Groups</b>	p1=0.019*,p2=0.213,p3=0.995,p4=0.731,p5=0.009*,p6=0.131						
<b>Inferior (um)</b>							
<b>Min. – Max.</b>	68.0 – 86.0	59.0 – 76.0	63.0 – 77.0	69.0 – 81.0			
<b>Mean ± SD.</b>	72.20 ± 5.37	68.05 ± 5.61	70.0 ± 4.14	74.85 ± 4.94	6.71		<0.001*
<b>Median (IQR)</b>	70.50 (69.0–73.50)	67.50 (65.0–73.0)	69.50(67.50–73.50)	75.0 (70.0–80.0)	4*		*
<b>Sig. bet. Groups</b>	p1=0.053,p2=0.517,p3=0.352,p4=0.615,p5<0.001*,p6=0.017*						
<b>Total (um)</b>							
<b>Min. – Max.</b>	67.0 – 87.0	62.0 – 76.0	63.0 – 77.0	70.0 – 79.0			
<b>Mean ± SD.</b>	73.05 ± 5.18	68.90 ± 4.83	70.65 ± 4.13	74.45 ± 3.56	6.11		0.001*
<b>Median (IQR)</b>	72.0 (70.0–73.50)	68.0 (65.50–74.0)	70.0 (68.0–74.0)	74.50 (71.0–78.0)	1*		
<b>Sig. bet. Groups</b>	p1=0.022*,p2=0.332,p3=0.755,p4=0.605,p5=0.001*,p6=0.043*						
<b>Inner plexiform layer (Gcl)</b>	Group (n=20)	I Group (n=20)	II Group (n=20)	III Group (n=20)	IV Group (n=20)	F	P
<b>Superior (um)</b>							
<b>Min. – Max.</b>	97.0 – 140.0	96.0 – 107.0	90.0 – 130.0	103.0 – 119.0			
<b>Mean ± SD.</b>	108.40 ± 11.23	102.30 ± 3.83	104.85 ± 8.30	109.15 ± 6.27	3.27		0.026*
<b>Median (IQR)</b>	106(105 – 107)	103(98.50–105.5)	105(101 – 109)	107.5(103 – 115)	5*		
<b>Sig. bet. Groups</b>	p1=0.077,p2=0.489,p3=0.990,p4=0.737,p5=0.037*,p6=0.319						
<b>Inferior (um)</b>							
<b>Min. – Max.</b>	98.0 – 133.0	90.0 – 107.0	90.0 – 128.0	101.0 – 119.0			
<b>Mean ± SD.</b>	106.75 ± 9.43	100.10 ± 5.04	105.10 ± 8.38	108.90 ± 6.92	4.83		0.004*
<b>Median (IQR)</b>	105(103.0–106.5)	100.5(99.0–102.5)	104.5(99.5–109.5)	108(102 – 115)	3*		
<b>Sig. bet. Groups</b>	p1=0.036*,p2=0.903,p3=0.809,p4=0.171,p5=0.003*,p6=0.398						
<b>Total (um)</b>							
<b>Min. – Max.</b>	99.0 – 136.0	94.0 – 107.0	90.0 – 129.0	103.0 – 119.0			
<b>Mean ± SD.</b>	107.55 ± 10.03	101.25 ± 4.05	104.85 ± 8.20	108.70 ± 6.30	3.91		0.012*
<b>Median (IQR)</b>	104.5(103.5–107)	102(99.0–103.5)	104.5(99.5–109.0)	106(103.0–115.0)	7*		
<b>Sig. bet. Groups</b>	p1=0.046*, p2=0.665, p3=0.962, p4=0.430, p5=0.012*, p6=0.370						



**Fig 2:** Correlation between LogMAR and inferior ganglion cell layer thickness

## Discussion

In the current investigation, there were significant difference between the groups based on both gender and age. In the examined groups, there were substantially more women than men. Age was considerably greater in group IV than the other three groups, group III than both group II and I, and group II than group I ( $P=0.001$ ).

In the same context with our results, previous authors examined 121 eyes from 121 healthy volunteers, including 72 females and 49 males. The average thickness of the lower quadrant RNFL was the highest at 129.32 µm, following the upper quadrant at 119.21 µm, nasal quadrant at 74.79 µm, and temporal quadrant at 64.72 µm. The research revealed a significantly different among the studied groups in terms of age<sup>[10]</sup>.

The examined groups had significantly different in IOP ( $P=0.032$ ). IOP was significant increase in group II than group IV ( $P=0.002$ ) while IOP was insignificantly different among the other studied groups.

Additionally, another study, observed that cross-sectional study of 3280 and found that IOP increased until the sixth decade of life, after which it decreased with increasing age, contributing to an inverted U-shaped pattern<sup>[11]</sup>.

Moreover, previous authors reported that IOP reduced from 13.9 mm Hg in those in their 60s to 13.1 mm Hg in those in their 70s, leading to the conclusion that IOP decreased with age, although somewhat IOP fell less in females and adult age groups than in males and younger age groups<sup>[12]</sup>.

The relationship among disc size, RNFL thickness, and the number of axons is controversial<sup>[13]</sup>. Despite the fact that some research have shown no link among disc size and RNFL thickness, others have found a favourable relationship between the two<sup>[14]</sup>.

In the same context with our results, previous authors examined the mean thickness of the cpRNFL taking into account their age and sex. Global cpRNFL thickness was measured at

91.2 ± 8.4 μm, with a range of 66.9 to 116 μm. Significantly, the average thickness of the cpRNFL in the inferior segment showed notable changes between the two age groups (p = 0.01 and 0.005 after Bonferroni correction), with the older age group displaying thinner measurements<sup>[15]</sup>.

Additionally, previous study found that there was a decrease of 0.365 μm in average RNFLT for each year advancing age (95% CI, 0.47-0.26) based on linear regression analysis, which was significantly (P < 0.001). This reduction in RNFLT with age was also confirmed by Spearman's correlation analysis (P < 0.05). Further analysis revealed that age-related decline in average RNFL was most pronounced in the lower quadrants, with a decrease of 0.575 μm per year (95% CI, 0.733-0.416; linear regression analysis, P < 0.001). These findings highlight the progressive age-related decline in RNFLT, with the most significantly decreased noticed in the lower quadrants, subsequently the upper, temporal, and nasal quadrants. The results provide valuable insights into the effect of age on RNFL thickness<sup>[10]</sup>.

Differences in the total average RNFLT between our research and previous research may be attributable to racial disparities between examined individuals. Normal Chinese, Latino, and Taiwanese eyes- were shown to have higher RNFLT values than Caucasian eyes in studies. Our study's homogeneously dispersed Turkish Caucasian population had a mean RNFLT of 97.01 μm, which was

somewhat lower than the published range of 98.1 to 101.5 μm according to TD-OCT<sup>[16,17]</sup>.

Research conducted by previous authors in Germany, it is worth noting that other factors such as axial length and refractive error might contribute to the differences in RNFLT observed in previous studies. Specifically, earlier studies using TD-OCT and SD-OCT have indicated that RNFLT tends to decrease with increasing severity of myopia<sup>[18]</sup>.

Furthermore, another study highlighted that in myopic eyes, eyeball elongation can lead to mechanical straining and thinning of the retina, leading to reduced RNFL. To mitigate the potential impact of severe myopia and longer axial length (greater than 25 mm), our study specifically selected participants within a narrow range of spherical equivalent, ranging from -1 diopters to +1 diopters. This selection criterion aimed to minimize the confounding effects of extreme myopia on RNFL thickness measurements in our study population<sup>[19]</sup>.

Previous authors showed a 0.43 μm/y drop in RNFLT in the upper quadrant (95 percent CI: 0.53–0.33) and a 0.29 μm/y decrease in the nasal region (95 percent CI: 0.39–0.18)<sup>[7]</sup>, values were comparable to those documented by previous report<sup>[6]</sup>.

Similar decreases in upper quadrant RNFLT- were found by another study [7] and in our investigation. Contrary to these results, another study observed a marked reduction in RNFLT in both the lower and upper quadrants. The

lower quadrants exhibited a reduction of 0.36  $\mu\text{m}/\text{year}$  (95% CI, 0.54–0.18), while the upper quadrants showed a reduce of 0.35  $\mu\text{m}/\text{year}$  (95% CI, 0.53–0.16). These findings indicate progressive thinning of RNFLT in both quadrants, as reported by previous authors<sup>[20]</sup>, and that they differed from those stated by another report<sup>[6]</sup>.

Similarly, , another study observed the drop in the lower quadrants was remarkable and doctors could be mindful in this declines<sup>[21]</sup>.

Based on the trial carried out by previous authors, the reduce in RNFLT varied across different quadrants. They reported a reduction of 0.488  $\mu\text{m}/\text{year}$  (95% CI, 0.646-0.330) in the upper quadrant, 0.575  $\mu\text{m}/\text{year}$  (95% CI, 0.733-0.416) in the lower quadrant, 0.253  $\mu\text{m}/\text{year}$  (95% CI, 0.350-0.156) in the temporal quadrant, and 0.141  $\mu\text{m}/\text{year}$  (95% CI, 0.272-0.01) in the nasal quadrant. A less dense papillomacular band could account for the restricted decrease in the temporal quadrant. Additionally, the ethnic characteristics may influence the variance of RNFLT throughout the four quadrants<sup>[10]</sup>.

Furthermore, another study found that there were variations in RNFLT across different racial groups. In their study, they observed regional differences in RNFLT across racial strata. On the other hand, Africans and Indians had significantly thinner RNFLT in the temporal nerve region corresponds with the papillomacular bundle compared to individuals of European descent. These results indicate that

racial differences can affect the variation of RNFLT in different quadrants of the retina<sup>[22]</sup>.

Persons of European descent had the thinnest RNFL values as measured by SD-OCT, whereas African Americans had the lowest RNFL scores in the temporal quadrant<sup>[23]</sup>.

Regarding superior, inferior and total Macular RNFL in the current work, similarly, previous authors discovered that the macular thickness of all individuals was 313.0  $\pm$  12.3  $\mu\text{m}$ , with a range of 277.6 to 371.1  $\mu\text{m}$ . The overall macular thickness of the inferior outer segment was significantly different between the age groups ( $p = 0.005$ )<sup>[15]</sup>.

Although the majority of research found a negative association between RNFLT and age, showing that RNFL thickness was reduced in elderly subjects, a few studies failed to demonstrate a meaningful link, perhaps due to the small number of subjects or the narrow range of ages of the subjects<sup>[24, 25]</sup>.

Regarding superior, inferior and total inner plexiform layer in the present work, previous authors found that the GCIPL thickness across various age and gender divisions. The median GCIPL thickness was 80  $\mu\text{m}$ , with an average of 80.3  $\pm$  5.6  $\mu\text{m}$  (range: 76.3 to 82.4  $\mu\text{m}$ ) and a minimum of 76.3  $\pm$  5.9  $\mu\text{m}$  (range: 63 to 90  $\mu\text{m}$ ). Both male and female participants had the greatest value in the supra nasal segment and the value with the lowest rank in the inferior segment. Age was shown to have a substantial influence on the average GCIPL thickness of each

segment, in their research. Age was related with a 0.29-m decline in the GCIPL thickness each year in old Korean participants<sup>[15]</sup>.

Previous research indicated that the linear decline in GCIPL thickness is from 0.14 to 0.30 m/year. Consistent with our findings, prior histological investigations have indicated that GCL and related axons (RNFL) are susceptible to loss with age<sup>[26,27]</sup>.

## Conclusion

The Retinal Nerve Fiber Layer Thickness (RNFLT) of healthy individuals was related to age, particularly in the temporal areas. There was insignificantly difference among the studied groups as regard (superior macular RNFL, inferior macular RNFL, and total macular RNFL). Age-associated RNFLT assessed in healthy participants using OCT was not detect the same slope in every sector/quadrant.

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