



Original Research Article

A cross-sectional analytical study to assess the correlation of myopia with ganglion cell complex and retinal nerve fibre layer thickness

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Abstract

Purpose: To evaluate the correlation between retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC) thickness in varying grades of myopia and emmetropia, and assess their reliability as diagnostic markers for glaucoma in myopic individuals using optical coherence tomography (OCT).

Materials and Methods: This cross-sectional study, conducted at Bharati Vidyapeeth Medical College, Pune, India (November 2022–January 2024), included 148 eyes from 59 myopic patients and 15 emmetropic controls. Participants underwent comprehensive ophthalmological examinations, including OCT scans to measure RNFL and GCC thickness. Myopes were categorized by spherical equivalent (Group A1: <-3D, A2: -3 to -6D, A3: >-6D) and axial length (Group B1: <23mm, B2: 23–24mm, B3: >24mm). Statistical analyses included Paired-T tests, ANOVA, and Pearson correlation tests ($P < 0.05$).

Results: Significant RNFL thinning was observed in myopes compared to emmetropes, particularly in the temporal quadrant for mild myopes and in nasal/inferior quadrants for moderate and severe myopes. RNFL thickness negatively correlated with increasing myopia and axial length ($P < 0.05$). Conversely, GCC thickness remained stable across all myopia grades and axial lengths, showing no significant correlation with spherical equivalent or axial length.

Conclusion: RNFL was reduced in all grades of myopia and axial length. GCC was not affected. This study effectively concludes that GCC is more reliable marker than RNFL thickness to assess glaucoma in myopes.

Keywords: Myopia, Retinal nerve fibre layer, Ganglion cell complex, Glaucoma, Spherical equivalent, Axial length.

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1. Introduction

Myopia is a refractive error that results from an elongation of the axial length or an increase in the refractive power of the eyeball. Worldwide, the prevalence of myopia is estimated to affect around 1.45 billion individuals.¹ Glaucoma is a progressive neurodegenerative disorder of raised intraocular pressure, optic disc changes and field abnormalities.^{2,3}

The structural changes in the optic nerve head and surrounding tissues associated with myopia make glaucoma diagnosis more difficult. The link between glaucoma and myopia is multifactorial, involving a combination of anatomical, genetic, and biomechanical factors. Myopic individuals have an increased risk of developing glaucoma.^{4,5} Myopia is a risk factor for primary open-angle glaucoma,

with myopic individuals being two to three times more likely to develop glaucoma later in life.⁶

Optical coherence tomography (OCT) is an essential diagnostic technique for evaluating Retinal nerve fibre layer (RNFL) thickness in glaucoma. Both the RNFL and ganglion cell complex (GCC) are key prognostic markers for monitoring the progression of glaucoma. Thinning of these structures is commonly seen in glaucoma.^{7,8}

Myopia can cause structural alterations in the inner retinal layers, often resulting in thinning. This poses a challenge in diagnosing and monitoring glaucoma in eyes with high myopia, as it becomes difficult to differentiate between glaucomatous changes and those caused by myopia.⁹⁻¹¹ This study aims to assess changes in RNFL and

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ganglion cell-inner plexiform layer (GCIPL) in myopic people using optical coherence tomography (OCT).

2. Aim

To evaluate and assess the correlation of RNFL and GCC thickness measurements in varying grades of myopia and emmetropia.

3. Objectives

1. To evaluate the RNFL and GCC thickness in varying grades of myopia
2. To evaluate RNFL and GCC thickness in varying grades of axial lengths
3. To find a correlation between RNFL and GCC thickness

4. Materials and Methods

4.1. Study design

This cross-sectional analytical study was carried out at Bharati Vidyapeeth Medical College and Hospital in Pune, India, over a 15-month period, from November 2022 to January 2024. The study was conducted in accordance with the ethical guidelines of the Declaration of Helsinki and received approval from the Institutional Ethics Committee. (Approval Number: BVDUMC/IEC99). All participants provided written informed consent after being fully informed about the study's purpose and procedures.

4.2. Procedure

A written informed consent was taken from all subjects before enrolling them in the study.

All participants underwent complete ophthalmological examination including: BCVA assessment, which was converted to a spherical equivalent, Slit-lamp examination, dilated fundus examination with a 90D lens and Indirect ophthalmoscope, IOP measurement with applanation tonometry and Axial length measurements using IOL master (Topcon).

All participants fulfilling the inclusion and exclusion criteria were divided into cases, that is 59 patients having myopia (based on their spherical equivalent) and 15 controls that is subjects with emmetropia (Spherical equivalent < -0.25 DS). Both eyes of all subjects were considered.

Myopes were divided in 2 groups: Group A and Group B depending on the spherical equivalent and axial length respectively.

Group A was further subdivided according to the grade of spherical equivalent as Group A1: < -3 D, A2: -3 to -6 D and A3: > -6 D.

Group B was further subdivided according to the axial length into Group B1: < 23 mm, B2: 23-24mm and B3: > 24 mm.

All myopes underwent two OCT scans by the Topcon OCT. RNFL was analysed by the 3D Disc mode in the glaucoma protocol. Ganglion cell complex thickness was analysed using the 3D Wide mode in the glaucoma protocol of the Topcon OCT. Average RNFL and RNFL thickness (in microns) of all quadrants was measured. Average GCC thickness (microns) and GCC thickness in the superior and inferior quadrant was measured.

Emmetropes (Group C) underwent RNFL OCT scan in the 3D Disc mode of glaucoma protocol. Average RNFL and RNFL thickness (in microns) of all quadrants was measured.

Littman's correction formula was applied to all the individual values.¹²

4.3. Statistical analysis

Data was entered into Microsoft Excel and statistical analysis was carried out in SPSS software version 17.0. Mean, standard deviation, minimum and maximum values were presented as quantitative variables.

RNFL values in myopes were compared to emmetropes using the paired-T test.

Variables like Axial Length, Spherical equivalent, RNFL and GCC were compared between Groups A and Group B using one way ANOVA test.

Average-RNFL and Average-GCC values were compared between all the groups using the Independent t-test.

RNFL and GCC values were compared between individual subgroups of Group and Group B using the independent t test. Confidence Interval (CI) of 95% was considered.

P value < 0.05 was considered as statistically significant.

Pearson correlation test was used to obtain a correlation between RNFL, GCC, spherical equivalent and axial length values. Correlation coefficient (r value) was calculated and P value < 0.05 was considered as a statistically significant correlation.

5. Results

148 eyes were selected for the study from 59 patients and 15 controls (emmetropes). Both eyes of all patients and controls were considered in the study. This study included 36 females and 23 males from 18-30 years age group (65% females and 35% males).

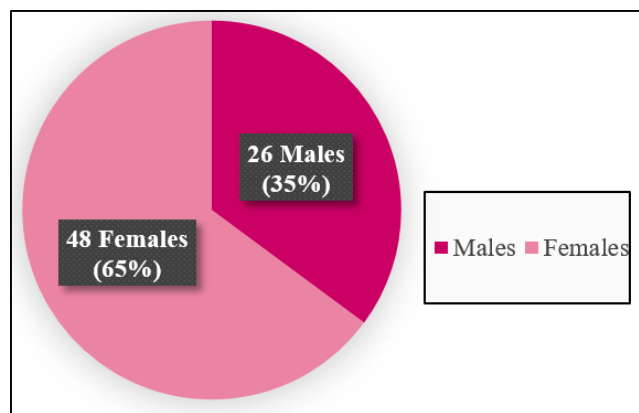


Figure 1: Demographic data

As per spherical equivalents,

Group A1 (<-3DS) n= 46, A2 (-3DS to -6DS) n= 37 and A3 (>-6DS) n=35

As per axial lengths,

Group B1 (<23mm) n=48, B2 (23mm to 24mm) n=42 and B3 (>24mm) n=38

Emmetropes (Group C) n=30

In the entire Group A, RNFL values ranged from 68.32 microns to 116.84 microns with an average RNFL of 100.15 microns and in the Controls (Group C), RNFL values ranged from 89.47 microns to 120.07 microns with an average RNFL of 101.6 microns.

5.1. RNFL in myopes and emmetropes

A statistically significant difference in average RNFL thickness was found between the control group and mild myopes in the temporal quadrant (SE < -3 DS). Additionally, significant differences in average RNFL thickness were observed between the control group and moderate myopes (SE between -3 DS and -6 DS), with changes evident in all quadrants except the superior quadrant. For severe myopes (SE ≤ -6 DS), significant differences in average RNFL thickness were noted across all quadrants, with the exception of the superior quadrant, when compared to the control group.

5.2. RNFL and spherical equivalent

There was a statistically significant difference in average RNFL thickness between mild and moderate myopes in both the nasal and inferior quadrants. A similar significant difference was observed between moderate and high myopes in terms of average RNFL value and thickness in the nasal and inferior quadrants. Additionally, a significant difference in both RNFL value and thickness was found between mild and high myopes, particularly in the inferior and nasal regions.

The average inferior and nasal RNFL values showed a statistically significant difference when all the myopia subgroups were examined.

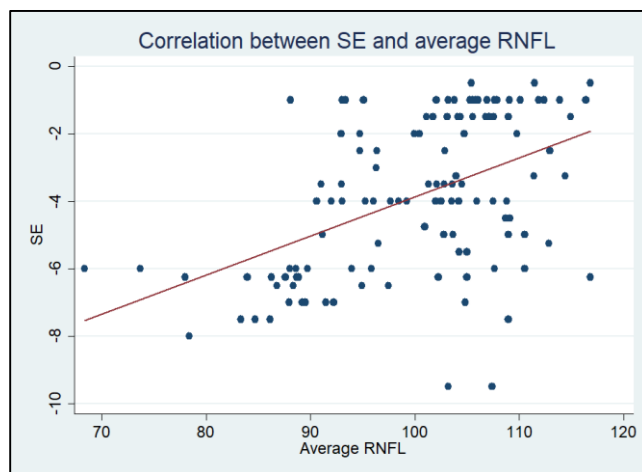


Figure 2: Correlation between spherical equivalent and RNFL

A negative correlation was seen when the average RNFL values were plotted against spherical equivalent. The average RNFL thickness significantly decreased as the myopia grade increased

5.3. GCC and spherical equivalent

Group A had GCC values ranging from 165 microns to 214 microns with an average of 203.89 microns.

No statistically significant difference was seen in the GCC values in Group A and in any of the quadrants when all the 3 sub-groups of Group A were compared.

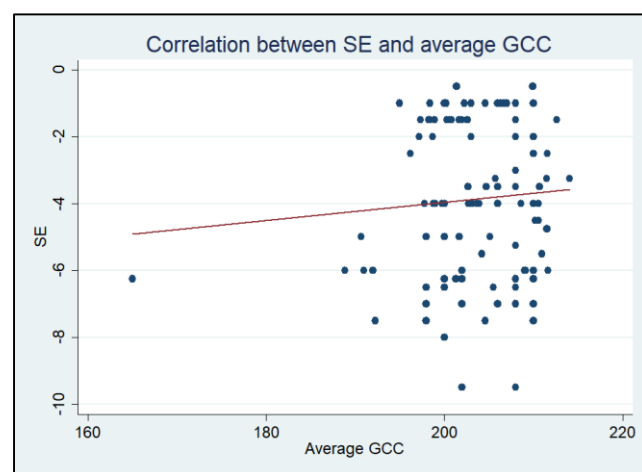


Figure 3: Correlation between GCC and spherical equivalent

In addition, no correlation was seen when the average GCC values were plotted against spherical equivalent (increasing grades of myopia).

5.4. RNFL and axial length

In the entire Group B, RNFL values ranged from 68.32 microns to 116.84 microns with an average RNFL of 100.15 microns.

The average RNFL values in the nasal and inferior quadrants as well as the average RNFL values between the

two groups showed a statistically significant difference. There was a statistically significant difference between the two groups' average RNFL values in the nasal and inferior quadrants. Both the average RNFL values and the average RNFL values in the nasal and inferior quadrants showed a statistically significant difference.

A statistically significant difference was observed in the average inferior and nasal RNFL values when all the subgroups of Group B were examined.

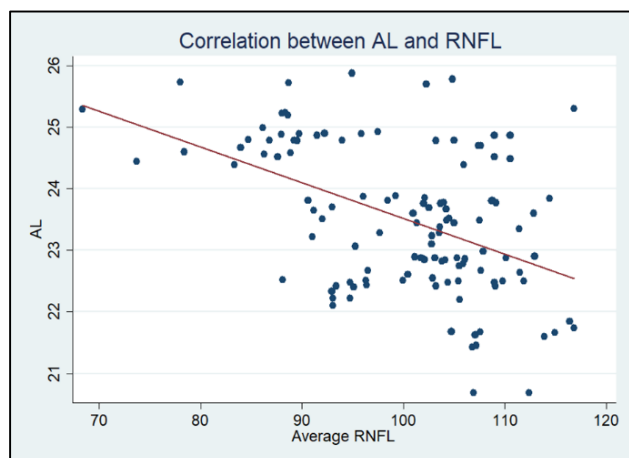


Figure 4: Correlation of RNFL and axial length

A negative correlation was seen when the average RNFL values were plotted against axial length. As the axial length increased, there was a thinning of average RNFL.

5.5. GCC and axial length

Group B had GCC values that ranged from 165 microns to 212.6 microns with an average GCC of 212.6 microns.

No statistically significant difference was seen in the GCC values in Group B and in any of the quadrants when all the 3 sub-groups of Group B were compared.

Table 1: RNFL thickness in individual group A1, A2, A3 and group C

Average RNFL(Microns)	Group A1 N=46	Group C N=30	p-value	Group A2 N=37	Group C N=30	p-value	Group A3 N=35	Group C N=30	p-value
Superior	127.3 ± 10.8	128 ± 12.1	0.296	127.1 ± 12.9	128 ± 12.1	0.37	121.1 ± 17.3	128 ± 12.1	0.439
Inferior	134.6 ± 8	132 ± 12.6	0.187	130 ± 9.2	132 ± 12.6	0.293	106 ± 9.3	132 ± 12.6	0.02
Temporal	78.7 ± 10.2	68.8 ± 8.3	<0	79.3 ± 11.9	68.8 ± 8.3	0.178	74.7 ± 15.5	68.8 ± 8.3	<0.001
Nasal	78.7 ± 8.1	76.4 ± 12.7	0.178	71.9 ± 12.5	76.4 ± 12.7	0.071	62.2 ± 9.8	76.4 ± 12.7	<0.001
Average	104.6 ± 6.7	101.6 ± 6.9	<0	102.2 ± 6.4	101.6 ± 6.9	0.008	92.1 ± 10.4	101.6 ± 6.9	0.03

Table 2: RNFL thickness in group A1 and A2, A2 and A3, A1 and A3

Average RNFL (microns)	Group A1 N=46	Group A2 N=37	p-value	Group A2 N=37	Group A3 N=35	p-value	Group A1 N=46	Group A3 N=35	p-value
Superior	127.3 ± 10.8	127.1 ± 12.9	0.92	127.1 ± 12.9	121.1 ± 17.3	0.1	127.3 ± 10.8	121.1 ± 17.3	0.07
Inferior	134.6 ± 8	130 ± 9.2	0.02	130 ± 9.2	106 ± 9.3	<0.001	134.6 ± 8	106 ± 9.3	<0.001
Temporal	78.7 ± 10.2	79.3 ± 11.9	0.82	79.3 ± 11.9	74.7 ± 15.5	0.17	78.7 ± 10.2	74.7 ± 15.5	0.17
Nasal	78.7 ± 8.1	71.9 ± 12.5	0.005	71.9 ± 12.5	62.2 ± 9.8	0.001	78.7 ± 8.1	62.2 ± 9.8	<0.001
Average	104.6 ± 6.7	102.2 ± 6.4	0.09	102.2 ± 6.4	92.1 ± 10.4	<0.001	104.6 ± 6.7	92.1 ± 10.4	<0.001

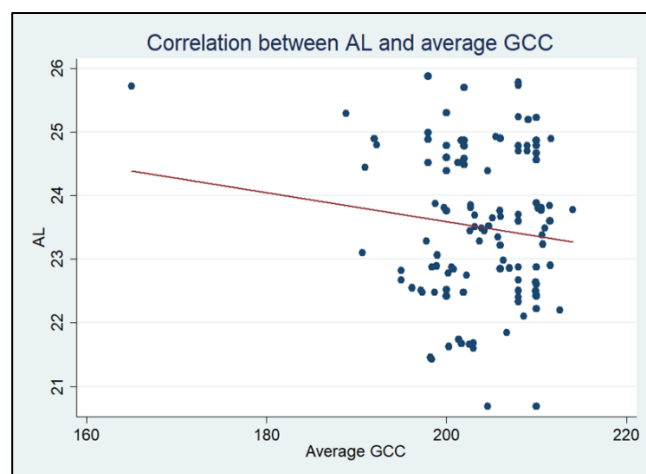


Figure 5: Correlation between GCC and axial length

In addition, no correlation was seen when the average GCC values were plotted against axial lengths.

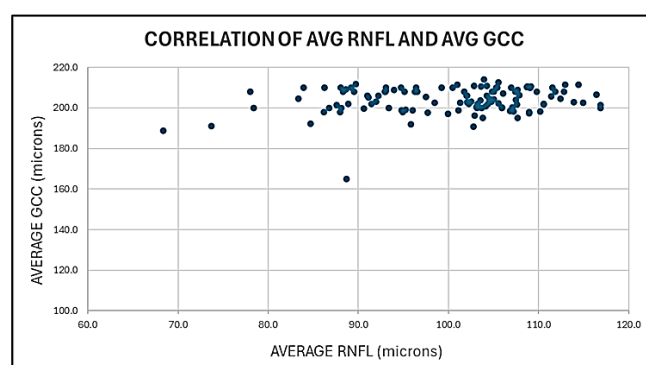


Figure 6: Correlation of AVG RNFL and AVG GCC

When the average RNFL was plotted against the average GCC for each spherical equivalent, average RNFL thickness decreased whereas average GCC thickness showed no significant change.

Table 3: RNFL thickness in the entire group A

Average RNFL (microns)	Group A1 N=46	Group A2 N=37	Group A3 N=35	p-value
Superior	127.3 ± 10.8	127.1 ± 12.9	121.1 ± 17.3	0.09
Inferior	134.6 ± 8	130 ± 9.2	106 ± 9.3	<0.001
Temporal	78.7 ± 10.2	79.3 ± 11.9	74.7 ± 15.5	0.25
Nasal	78.7 ± 8.1	71.9 ± 12.5	62.2 ± 9.8	<0.001
Average	104.6 ± 6.7	102.2 ± 6.4	92.1 ± 10.4	0.96

Table 4: GCC thickness in group A and in groups A1 A2 A3

Average GCC (microns)	Group A1 N=46	Group A2 N=37	Group A3 N=35	p-value
Superior	203.7 ± 4.8	204.7 ± 4.6	204.3 ± 5.1	0.63
Inferior	203.7 ± 5.7	205.1 ± 4.5	204.4 ± 4.9	0.47
Average	204 ± 5.1	205 ± 5	203.4 ± 6.3	0.42

Table 5: RNFL thickness in group B1 and B2, B2 and B3, B1 and B3

Average RNFL (microns)	Group B1 N=48	Group B2 N=32	p-value	Group B2 N=32	Group B3 N=38	p-value	Group B1 N=48	Group B3 N=38	p-value
Superior	126.8 ± 11.1	123.2 ± 16.4	0.28	123.2 ± 16.4	125.6 ± 14.7	0.51	126.8 ± 11.1	125.6 ± 14.7	0.68
Inferior	134.5 ± 8	123.8 ± 14.4	<0.001	123.8 ± 14.4	112.9 ± 14.1	0.002	134.5 ± 8	112.9 ± 14.1	<0.001
Temporal	77.9 ± 9.9	75 ± 13.3	0.29	75 ± 13.3	79.7 ± 14.7	0.17	77.9 ± 9.9	79.7 ± 14.7	0.54
Nasal	77.4 ± 9.4	71.3 ± 12.8	0.03	71.3 ± 12.8	64.7 ± 11.2	0.03	77.4 ± 9.4	64.7 ± 11.2	<0.001
Average	103.9 ± 6.9	98.6 ± 10.4	0.01	98.6 ± 10.4	96.6 ± 10	0.41	103.9 ± 6.9	96.6 ± 10	<0.001

Table 6: RNFL thickness in entire group B

Average RNFL (microns)	Group B1 N=48	Group B2 N=32	Group B3 N=38	p-value
Superior	126.8 ± 11.1	123.2 ± 16.4	125.6 ± 14.7	0.52
Inferior	134.5 ± 8	123.8 ± 14.4	112.9 ± 14.1	<0.001
Temporal	77.9 ± 9.9	75 ± 13.3	79.7 ± 14.7	0.3
Nasal	77.4 ± 9.4	71.3 ± 12.8	64.7 ± 11.2	<0.001
Average	103.9 ± 6.9	98.6 ± 10.4	96.6 ± 10	0.66

Table 7: GCC thickness in groups B1 B2 B3

Average GCC (Microns)	Group B1 N=48	Group B2 N=32	Group B3 N=38	p-value
Superior	203.61 ± 4.6	203.05 ± 4.6	205.18 ± 7.2	0.255
Inferior	203.58 ± 5.4	203.53 ± 4.4	204.91 ± 8.6	0.573
Average	203.88 ± 4.9	202.4 ± 6.2	205.04 ± 7.9	0.233

6. Discussion

Globally, myopia is the primary cause of vision impairment and a significant public health concern. Adults between the ages of 10 and 20 are estimated to have a prevalence of high myopia of 10–20% worldwide.^{13,14} The annual incidence of myopia in India is 3.4% and prevalence of myopia in India is 21.1%.¹⁵ The prevalence of glaucoma worldwide is 3.54% and in Asia it is 1.09%.^{16,17}

Glaucoma causes thinning of the RNFL and GCC layers. Myopia is a risk factor for glaucoma. Myopes are more prone to develop glaucoma. It is postulated that myopes have a thinned out RNFL.^{4,5,7,18} Hence, analysis of RNFL thickness

alone in myopia for the evaluation of glaucoma can be fallacious and lead to a wrong diagnosis of glaucoma.

This study which correlates RNFL and GCC thickness with increasing grades of myopia and axial length aims to prove that GCC thickness measurement is a more reliable indicator of the diagnosis of glaucoma in myopic patients.

6.1. Comparison of RNFL thickness between myopes and emmetropes

We found that the average RNFL thickness in emmetropes in our study was 101.6 ± 6.9 microns which was comparable with the global normative data of emmetropes that is 97.3 ± 9.6 µm and in Asia is 100.7 ± 8.5 µm.¹⁹

We compared the average RNFL thickness in myopes with emmetropes and found that, a significant thinning of average RNFL was seen in all grades of myopia (significance<0.05). A case control study between myopes and emmetropes (controls), conducted by Dongmei et al in China which showed a similar significant thinning of average RNFL in myopes when compared with emmetropes.²⁰

When individual quadrants of RNFL were evaluated, we saw that the Retinal nerve fibre layer thickness in the temporal quadrant showed significant thinning as compared to the values in controls in the low myopia group (<-3DS).

No significant thinning was noted in any quadrant of the moderate myopia group (-3DS to -6DS), though the average RNFL thickness was significantly less as compared to the emmetropic group.

However, thinning of RNFL was seen in all quadrants except the superior quadrant in the group of high myopes (>-6DS). A study conducted by Sang min park et al in South Korea compared RNFL thickness between myopes and controls, showed RNFL thinning in the inferior and nasal quadrants in all grades of myopia when compared with emmetropia.^{21,22}

6.2. Comparison of RNFL thickness between all the grades of myopia

When we compared the average RNFL values in each individual grade of myopia with each other and found that a significant thinning of average RNFL between moderate grade and high myopia ($p < 0.001$) and also between low grade and high degree myopia ($p < 0.001$). No significant thinning of average RNFL was seen between low and moderate myopia.

A similar significant difference of average RNFL between varying grades of myopia was detected in a study conducted by Ganekal S et al in Bengaluru, India. Similar finding was noted by Sang et al in South Korea.^{21,23}

We found that a significant difference between the RNFL values of the inferior and nasal quadrants was seen between all 3 grades of myopia. No significant change in the temporal quadrant was noted in any grade of myopia. This is of special significance in diagnosis of myopia where RNFL loss follows the ISNT rule.

Ganekal S et al and Seo S et al also found a significant thinning of RNFL in the inferior and nasal quadrants.^{23,24} Studies conducted by Porwal S et al in Bengaluru, India also found significant reduction in the RNFL thickness.²⁵

6.3. Comparison of RNFL thickness between all the groups of axial length

There was a negative association between axial length and RNFL thickness. The average RNFL thickness decreases as the grades of axial length increase. Significant RNFL

thinning was noted in the inferior and nasal quadrants of all groups.

Studies by Mishra A et al in Orissa and Savini G et al in Italy showed that average RNFL was significantly reduced.^{26,27}

6.4. Comparison of GCC thickness between all the grades of myopia and groups of axial length

The average GCC thickness measured in our study was 203.89 microns which was comparable with the global normative data of 150-250 microns. GCC values ranged between 165 microns to 214 microns in the entire study sample.²⁸

No significant variation was seen in the GCC thickness with increasing grades of myopia (spherical equivalent). Various studies have shown conflicting results about GCC thickness and increasing grades of myopia

Study conducted by Porwal S et al. in Bengaluru, found that the average GCC values were significantly reduced as the grades of myopia increased.²⁵ Ganekal S et al concluded that GCC thickness was significantly affected as grades of myopia increased. But no significant change was detected on analysis of the various quadrants in either group.²³

We found that no significant change was noted in the average or quadrant GCC thickness as the axial length increased.

Few studies are available that have analysed GCC thickness with increasing grades of myopia. Our study shows that since GCC thickness is not significantly affected in myopes.

We thus conclude that as GCC thickness is not significantly reduced in any grade of myopia or axial length, it could be considered a more reliable indicator of assessing glaucoma in myopes.

7. Limitation

Higher myopes (>-7DS) had poor centration on the OCT machine causing poor image quality of the scans. Such scans had to be excluded, and these subjects couldn't be enrolled in the study.

8. Conclusion

The average retinal nerve fiber layer (RNFL) thickness is reduced across all degrees of myopia, with thinning observed even in those with low myopia (<-3D) and axial lengths under 23mm. A negative correlation was found between average RNFL thickness, spherical equivalent and axial length indicating a reduction in RNFL thickness with increasing grades of myopia and increasing axial lengths.

In contrast, ganglion cell complex (GCC) thickness remained unchanged across different levels of spherical

equivalent or axial length, indicating that GCC thickness is not significantly affected by the severity of myopia or axial elongation.

Since myopic patients are more prone to developing glaucoma and already exhibit RNFL thinning, there is a risk of misdiagnosis if RNFL thickness is the sole factor considered. Given that GCC thickness is not significantly influenced by myopia or axial length, it should be regarded as a more reliable and important marker for diagnosing and monitoring glaucoma in myopic individuals. This study effectively proves that GCC thickness measurement is a more reliable and an accurate marker than RNFL thickness in assessing the progress of glaucoma in myopes.

9. Source of Funding

None.

10. Conflict of Interest

None.

11. Ethical Approval

Ethical No. BVDUMC/IEC/99.

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