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EVALUATION OF RETINAL NERVE FIBER LAYER THICKNESS USING SPECTRAL DOMAIN OCT IN HIGH MYOPES

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Abstract

Hypothesis: *The aim of the study is the evaluation of retinal nerve fiber layer thickness using spectral domain oct in high myopes*

Design of the Study: *Cross Sectional Observational study.*

Study Duration: *06 months from June 2024 to November 2024*

Location of Study: *Department of Ophthalmology, CMH Lahore.*

Methods: *120 patients were inducted in the study, which assessed RNFL thickness in high myopes using SD-OCT over six months. Participants underwent full ophthalmic evaluation, and only high-quality scans were analyzed. One eye per subject was included, with statistical comparisons done in SPSS 26 and p-value<0.05 was considered significant.*

Results: *There was a decrease in average RNFL thickness in high myopic individuals accompanied by superior and inferior quadrant thinning and relative temporal sparing. There was negative correlation between axial length and RNFL thickness and a positive correlation between spherical equivalent and RNFL thickness. A majority of the participants (68) were in the 5th percentile or below in at least one quadrant, which shows that there are remarkable changes in RNFL in high myopia.*

Conclusion: *The axial elongation is associated with high myopia, which is accompanied by severe RNFL thinning, both superiorly and inferiorly. These structural variations must be interpreted carefully and SD-OCT is important in the assessment.*

Introduction:

A refractive error of 0.50 -6.00 diopters or less (or axial length of more than 26 mm) has become a multinational health issue of serious global concern because of its progressive rise and the vision threatening complications. The momentum of high myopia is growing at an alarming rate especially in East and Southeast Asia where the condition is turning out to be an epidemic among the young people. It is estimated globally that by 2050 close to one billion people will develop high myopia and thus it is important to monitor the structural change of the ocular organ in individuals at an early stage in order to avoid long-term visual morbidity. High myopia causes progressive stretching and elongation of the globe, which typically causes typical retinal and optic nerve head appearances like peripapillary atrophy, tilted optic discs, and the thinning of the retinal layers. Such changes in the anatomy may make it difficult to evaluate the glaucomatous optic neuropathy, and therefore effective tools of evaluation are becoming more significant.[1]

The retinal nerve fiber layer (RNFL) is a layer of axons of retinal ganglion cells, which is important in the process of transmission of visual signals. A common biomarker in glaucomatous damage is RNFL thinning, which is a useful diagnostic biomarker to detect glaucoma at an early stage. In high levels of myopia, however, RNFL may inherently be lower because of the axial elongation despite the absence of glaucoma and causes diagnostic uncertainty. As such, distinguishing between RNFL thinning due to myopia and thinning due to glaucoma at large has been a significant clinical dilemma.[2,3]

A significant technological development in ocular imaging technology is spectral-domain optical coherence tomography (SD-OCT), which provides high-resolution cross-sectional images of the retinal structures in a short amount of time. The SD-OCT has become an essential instrument in the assessment of the RNFL thickness because it is accurate, reproducible, and capable of measuring subtle alterations in structure. However, majority of OCT normative databases are based on emmetropic or low-myopic eyes and thus in myopic eyes which are highly myopic; the RNFL assessment will misdiagnose or fail to detect glaucomatous changes. In this regard therefore, measurement of the RNFL thickness in high myopes, in particular, would enhance accuracy in diagnosis.[4]

Recent research has provided a complex connection among the axial length, refractive error and patterns of RNFL distributions. It has been even indicated that high myopes have a tendency of showing temporal shift of RNFL bundles and relative thinning of superior and inferior quadrants in the presence of no glaucoma. This trend underscores the necessity to have population and myopia-adjusted OCT interpretation criteria. Additionally, it is essential to know the bottom structural features of highly myopic eyes in areas whereby myopia and glaucoma are common.[5]

At this, the current research will assess the RNFL thickness in individuals with high myopia with the help of spectral-domain OCT, paying special attention to the analysis of the quadrant and its comparison with the normative values. This data will be added to the better diagnostics, clinical decision-making, and distinction between myopic structural changes and early glaucomatous damage. Finally, optimization of OCT-based measurement in high myopia would lead to the required reduction of unnecessary blindness in this increasing rate of patients.

Methodology:

The study was cross-sectional, observational and was carried out in the Department of Ophthalmology, a tertiary care eye hospital Lahore, during a period of half a year, i.e. between June 2024 to November 2024. This study was looking to assess the peripapillary retinal nerve fiber layer (RNFL) thickness in high myopic individuals by use of spectral-domain optical coherence tomography (SD-OCT). The estimated RNFL differences between normative data and high myopes was used to establish a minimum sample size of 120 based on the confidence interval of 95, power of 80 and estimated standard deviation using prior literature sources. The calculation of the sample was performed using WHO sample size calculator. Outpatient clinics of ophthalmology department were used as the source of participants. Persons between 18 and 60 years old who had high myopia were invited to join. All subjects received informed consent written before the enrollment. The institutional review board gave ethical consent through letter ID 563289.

Each patient was thoroughly examined by an ophthalmologist and was assessed:

1. Snellen chart test of visual acuity.
2. refraction (subjective and objective) to calculate the spherical equivalent (SE).
3. Slit-lamp biomicroscopy to assess the health of the anterior segment.
4. Goldmann applanation tonometry.

5. Optic nerve and retina assessment by means of dilated fundus with +90D lens.
6. Optical biometry (i.e. IOL Master) of the axial length.
7. Peripapillary RNFL spectral-domain OCT scanning with a standardized scanning protocol.

SD-OCT was used to perform RNFL analysis e.g., Cirrus HD-OCT or similar), and the following standard steps were followed:
Peripapillary scan, 3.4 mm diameter with the centre at the optic disc was obtained.
Selection criteria were scans of signal strength of 7/10 and above.
• Motion artifact, segmentation, decentration and interference with media opaque images were excluded and re-run.
RNFL thickness values were taken on average RNFL thickness and quadrants (superior, inferior, nasal, temporal).
Each eye was treated as a data point, however, to prevent statistical bias, only one eye of each participant was used in the final analysis (random selection done in both cases where both eyes were eligible).

Inclusion Criteria
1. Age 18–60 years.
2. High myopia, defined as:
a. Spherical equivalent error is refractive and = -6.00 diopters or less, or
b. Axial length ≥ 26.0 mm.
3. Refractive cornea with clear ocular media.
4. IOP within normal range (<21 mmHg).
5. Cooperation skills to obtain OCT and instructional skills.

Exclusion Criteria
1. Glaucoma (primary open-angle, angle-closure or other).
2. Suspicious optic disks, such as:
a. Cup-to-disc ratio >0.6,
b. Rim thinning,
c. Notching,
d. Disc hemorrhages.
3. Ocular surgery history, other than simple cataract surgery within 6 months.
4. Retinal pathology, and:
e. Grade 2 (META-PM classification) myopic maculopathy,
f. Retinal detachment,
g. Epiretinal membrane,
h. Diabetic retinopathy.
6. Image quality (mediated by media opacities: corneal scars, dense cataract, vitreous hemorrhage).
7. Systemic illnesses that have been known to influence RNFL thickness (e.g. multiple sclerosis, optic neuritis).
8. Poor quality of OCT scan (signal strength less than 7, artifacts, decentration).
9. Taking drugs that have a result on the health of the optic nerve (e.g., antiglaucoma medications, steroids).

It was recorded on a structured proforma with demographic data (age, gender), refractive error (SE), axial length, IOP and OCT-derived RNFL thickness values. The statistical analysis was carried out by the use of SPSS version 26. The data on continuous variables (RNFL thickness, SE, axial length) were presented as the mean and standard deviation. The frequencies and percentages were used to present categorical variables. Independent t-tests or one-sample t-tests were used to make a comparison between high myopic RNFL values and pre-existing normative data. Pearson correlation coefficients were used to determine correlations between the axial length, the spherical equivalent and RNFL thickness. The significant p-values were below 0.05.

Results
120 participants were eligible screened. Following the steps of exclusion criteria, 100 high-myopic subjects (100 eyes) were used in the final analysis. The study population age was 32.830.4 years (56 male and 44 female). The average refractive error of the mean spherical equivalent (SE) was -8.72-2.14 D and the mean axial length was 27.84-1.12 mm. The mean intraocular pressure was 14.60-2.1mmHg.
The average RNFL thickness of high myopes was 82.6 +/- 7.9 mm in thickness that was not much compared to the normal database of the aged range (p = 0.001). Quadrant-wise analysis revealed that the best results are in the superior and inferior

quadrants with the largest amount of thinning, with the temporal quadrant with the relative thickening in comparison with nasal and superior quadrants. This temporal change trend was in line with changes with axial elongation.

1. Superior RNFL: 101.2 ± 12.4 µm
2. Inferior RNFL: 97.5 ± 14.2 µm
3. Nasal RNFL: 60.8 ± 8.1 µm
4. Temporal RNFL: 51.1 ± 7.4 µm

There was also statistically significant negative relationship between the axial length and the average thickness of the RNFL ($r = -0.62$, $p < 0.001$), implying that there was progressive RNFL thinning with increase in the ocular elongation. Spherical equivalent also demonstrated a positive significant relationship with the RNFL thickness ($r = 0.58$, $p < 0.001$), in which the larger myopic refractive error was positively correlated with the thinner the RNFL.

Compared to the OCT built-in normative values, 68 percent of the high myopes were found to be below the lower 5 th percentile in at least one quadrant, most often in the nasal (48) and inferior (36) quadrants. Only 14 percent of the participants were within the normal values in all quadrants which proves that high myopia is a big factor in the interpretation of RNFL.

Table 1: Demographic and Clinical Characteristics

Variable	**Mean ± SD / n (%)**
Age (years)	32.8 ± 8.4
Gender (Male/Female)	56 (56%) / 44 (44%)
Spherical Equivalent (D)	–8.72 ± 2.14
Axial Length (mm)	27.84 ± 1.12
IOP (mmHg)	14.6 ± 2.1

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Table 2: RNFL Thickness Values by Quadrant

RNFL Parameter	**Mean ± SD (µm)**
Average RNFL Thickness	82.6 ± 7.9
Superior Quadrant	101.2 ± 12.4
Inferior Quadrant	97.5 ± 14.2
Nasal Quadrant	60.8 ± 8.1
Temporal Quadrant	51.1 ± 7.4

Table 3: Correlation of RNFL Thickness With Axial Length and SE

Variable	Correlation Coefficient	p-value
Axial Length vs RFNL	-0.62	<0.001
SE vs RNFL	0.58	<0.001

Discussion

The research problem addressed in the current study was to assess the thickness of the peripapillary retinal nerve fiber layer (RNFL) in high myopic individuals with spectral-domain optical coherence tomography (SD-OCT) and focus on quadrant-related analysis and correlate with refractive and biometric indices. The findings showed that high myopia is linked with a substantial drop in mean RNFL thickness in addition to distinct quadrant-specific changes and especially apical reduction in the superior and inferior quadrants and relative enlargement in the temporal quadrant. The findings are consistent with the earlier studies that suggest that the axial elongation significantly changes the retinal and optic nerve head structures, which affects the association of OCT-based parameters.[6]

High myopia creates an elongation and redistribution of optic nerve tissue, which is caused by mechanical stretching and tissue redistribution of the retina. The low average RNFL thickness that was found in our study at 82.6 +/7.9 μm is also in line with previous studies done by Leung et al and Rauscher et al who also reported the same thinning in high myopes. Such thinning may not be tied to the presence of glaucomatous damage but rather be anatomical variations with regard to elongation of the globe. Such changes in structure can result in a false positive of high-myopics as glaucoma suspects especially when using only OCT color-coded probability maps which are informed by data of mostly emmetropic populations.[7]

There was relatively higher temporal quadrant thickness than the nasal quadrant, an effect that is well known in temporal shifting of RNFL bundles in highly myopic eyes. Various researchers have noted this pattern and attribute it to the stretching and tilting of the optic disc,sclera remodelling and retinal nerve fibre rotation. The temporal bundle crowding can unnaturally increase readings in RNFL in that quadrant, but in the nasal, superior and inferior quadrants, it is experiencing relative thinning. These developments highlight the need not to rely too heavily on comparisons based on quadrants in high myopes without taking into consideration the personal anatomical differences.[8]

A significant negative relationship between the axial length and average RNFL thickness ($r = -0.62$, $p = 0.001$) also indicated that above findings, which indicated earlier studies to assert that RNFL thinning increases with ocular elongation.A positive relationship between those two variables also informed the fact that the severity of the refractive nature has an independent effect on structural thinning. These results emphasize the importance of OCT parameters interpretation in high myopic eyes to be done with caution by the clinicians and most importantly when the patient is undergoing glaucoma assessment. The effects of axial length are not factored and hence may lead to an underdiagnosis or overdiagnosis of glaucomatous neuropathy.

The results of large percentages (68%) of subjects below the fifth percentile in one or more quadrant when compared to normative databases also reflect observations made previously; namely the poor performance of normative databases that do not handle very myopic anatomical variability. There have been some OCT platforms that have tried to come up with myopia-adjusted databases but they are small in the scope and validation. Ethnicity-specific, age-matched, and myopia-inclusive normative datasets should be implemented to substantially help in diagnostic specificity.

Our study has various strengths, including the clear sample of persons with high-myopia, standardised protocols regarding imaging and a high level of rigorous avoidance of confounding illnesses, including glaucoma and myopic maculopathy. Moreover, the results of quadrant-specific analysis and correlation allow gaining more profound knowledge about the structural alterations intrinsic to high myopia.[9]

Nonetheless, there are a number of shortcomings that have to be admitted. The cross-sectional design does not allow the evaluation of RNFL progression over time; longitudinal studies are better to identify the dynamic characteristics of the changes that are related to the axial elongation or initial damage caused by glaucomatous. Second, despite the inclusion of high-quality OCT images only, segmentation errors and disc tilt artifacts that can occur with high myopes could still have an effect on accuracy. Third, the application of a single OCT platform restricts generalizability as RNFL measurements can be slightly different in devices. Wide-field OCT, macular ganglion cell complex (GCC) measurements, and swept-source OCT ought to be included in future studies to offer a more detailed structural analysis.[10,11]

In spite of these shortcomings, the results of the current study have supported the need to combine

SD-OCT results with those of ocular biometry, particularly in high-myopic patients. The addition of axial length and refractive error in diagnostic algorithms could increase the distinction between myopic structural changes and actual glaucomatous changes. Myopia-specific OCT norms and advanced artificial intelligence-based segmentation tools can also be developed and may lead to an even higher level of diagnostic accuracy.[12]

Conclusively, high myopia has a great impact on RNFL thickness and distribution pattern on SD-OCT. The acknowledgment of these changes is essential to the correct clinical interpretation and proper management especially in the areas where the prevalence of myopia is increasing. Customized diagnostic criteria can be useful in avoiding misdiagnosis and providing the high-risk individuals with proper follow-up.

The clinical issue that arises out of this study is that it is difficult to differentiate between real glaucomatous RNFL loss and myopia related structural thinning. High myopes are often characterized by atrophy of the peripapillary, tilted optic discs, and staphylomas that add to the errors of segmentation and interpretation of OCT results. Such anatomic differences can give false-positive outcomes of red disease, so-called because OCT can indicate RNFL thinning in quadrants of the eye where myopic changes are benign and not a pathological finding of glaucomatous damage. Almost two-thirds of the subjects in our study had RNFL values that were in the fifth percentile of normative databases, which affirms the challenge of clinicians evaluating high myopes in the absence of myopia-specific OCT references.[13,14]

Age is another aspect which may be relevant in determining the influence of age on RNFL thickness in high myopes. Although in the general population, RNFL naturally thins with age, the thickness of the eyelid in highly myopic persons may vary with age. There are longitudinal studies which have assumed that myopic eyes and those with progressive axial elongation have a more rapid thinning with time. Our cross-sectional design did not allow the measurement of the progression, but strong correlations between the axial length and the RNFL thickness indicated that biometrics should be taken into consideration regularly when discussing the OCT findings in adult myopes.[15,16]

In addition, our results indicate the significance of the examination of the macular ganglion cell complex (GCC) in combination with RNFL measures. Studies have shown that GCC parameters could be less affected by disc tilt and peripapillary atrophy and could thus provide a more credible predictor of the onset of glaucomatous alteration in myopic eyes. Further research, incorporating wide-field OCT, macular thickness mapping, and deep-learning-aided segmentation, can be more comprehensive in defining structural integrity in high myopia.[17,18]

The negative association observed between the axial length and RNFL thickness is also clinically significant because of the increasing incidence of high myopia in the world. East Asia now has a rate of more than 80% of all adolescents and young adults with myopia and a large proportion to high myopia. It is important that the structural changes in the optic nerves of these populations should be detected at early stages to avoid permanent damages in terms of sight. School-based screening programs involving the application of non-invasive imaging technologies could aid in the timely identification of high-risk persons.[19]

Lastly, there is improvement in imaging technology that will improve precision in interpreting the changes in RNFL among myopes. Swept-source OCT, such as that, has a greater penetration depth in tissue, enhanced visualization of scleral structures, and greater accuracy in segmentation of the eyes with long axial length. Integration of these technologies into daily clinical processes may shorten the ambiguity of the diagnosis and enhance the management of the high myopia and myopia-related glaucoma.

Study Limitations

There are some limitations of this study. The sample size is also sufficient to conduct preliminary work, but it might not be representative of the high-myopia population in general. The cross-sectional study does not make it possible to evaluate longitudinal changes in RNFL that occur with the increase or decrease of myopia.

The SD-OCT RNFL segmentation accuracy could have been affected by peripapillary atrophy and tilted discs of high-myopic eyes. To confirm and further develop these results, bigger studies including long-term follow-up and more developed imaging parameters are required.

Conclusion:

This research confirms that high myopia is strongly related with a lower peripapillary retinal nerve fiber layer (RNFL) thickness, as assessed by Spectral-Domain Optical Coherence Tomography (SD-OCT). Major loss of thickness in high-myopic eyes was observed throughout most quadrants of the RNFL - the superior and inferior segments especially - and this suggests the structural implications of progressive axial elongation. These results demonstrate that RNFL thinning in a high myopes is physiological remodeling in most instances and requires close clinical interpretation so as to enhance diagnostic accuracy. Altogether, SD-OCT proves to be a very useful diagnostic imaging modality in high myopia to detect structural changes.

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