Retinal Nerve Fiber Layer Thickness in Recently Diagnosed Primary Open Angle Glaucoma

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ABSTRACT

Purpose: To determine the frequency and pattern of retinal nerve fiber layer thinning in recently diagnosed primary open-angle glaucoma (POAG).

Methodology: This Cross-sectional study was carried out at the Ophthalmology Department, Hayatabad Medical Complex Peshawar from 1st May, 2021 to 31st March, 2022. Patients with a history of POAG were included in the study and subjected to assessment of visual acuity, IOP with Goldman Applanation Tonometer (GAT) and Global retinal nerve fiber thickness (G-RNFL) through OCT. RNFL thickness was further stratified by age and gender to explore effect modification, employing ANOVA for age group comparisons, and t-tests for RNFL thinning, with a significance level set at $p < 0.05$.

Results: A total of 136 patients with a history of POAG were recruited. The mean age of the study sample was 54.5 ± 13.6 years. There were 66.9% males and 33.1% females. The mean duration of POAG was 239.2 ± 106.1 days. The mean BCVA was 0.696 ± 0.7 and IOP was 18.9 ± 9.1 mmHg. The Retinal nerve fiber thickness (RNFL) was 65.4 ± 22.2 microns and 50.7% had their right eye with worse involvement. The G-RNFL thickness varied among the patients, with the majority in the age group 55–80 years having a mean thickness of 65.4 ± 22.3 microns, which, along with the overall G-RNFL thickness of 65.18 ± 22.97 microns, did not show statistical significance (p-values of 0.329 and 0.986, respectively).

Conclusion: Global retinal nerve fiber thickness is a significant prognostic factor for POAG.

Key Words: Glaucoma, Visual acuity, Intraocular pressure, Retinal Nerve Fiber Layer.

INTRODUCTION

While debate on the many theories of Glaucoma is still as relevant as it was perhaps when Donders coined the term in 1862; several characteristics have become clearer with time. Namely, there is neurodegeneration of the optic nerve with characteristic visual defects and a peculiar association with intra-ocular pressure.[1] Another profound yet often underrated feature is the orderly loss of nerve fibers and decrease in thickness on diagnostic modalities.[2] This apoptosis of the nerve fibers has characteristically been in a peripheral to

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central pattern regardless of the type or cause of Glaucoma. The Vision Expert Loss Group (VLEG) has reported that glaucoma is the second leading cause of blindness from all possible causes of blindness with age-standardized prevalence of total blindness in adults 50 and over of 11.0% (9.3-12.8,95% uncertainty intervals).[3] This is second only to cataract which is classically much more straightforward to treat compared to the convoluted pathophysiology of glaucoma effectively making it the leading cause of irreversible blindness worldwide. Insights from Global Burden of Diseases, Injuries, and Risk Factors Study (GBD 2017) revealed a prevalence of 0.03% (0.03-0.04, 49% female) for Pakistan as well a steady rise in all-age prevalence.[4]

Early detection of glaucoma by any means whether examination or diagnostic is imperative in improving patient visual outcome and stopping progression of the disease.[5,6] This is especially crucial because any damage to the optic disc and retinal nerve fiber layer is irreversible in case of late detection, inadequate treatment with some degree of varying individual variation among patients. The Optical Coherence Tomography (OCT) remains one of the most valuable glaucoma detection tools among newer technologies and machine learning tools because of its comparatively wide spread availability.[7] The fact that it is non-invasive and relatively straightforward to perform and interpret is also a plus in high volume practices.

In our study we have studied RNFL thickness, visual acuity, Intraocular pressure as well as demographic variables like age and gender. The relationship between these factors has been extensively studied and documented, highlighting the irreplaceable role of RNFL thickness as diagnostic, prognostic, and monitoring utility in glaucoma management.[8] It provides essential parameters in helping clinicians distinguish anatomical changes which are borderline on dilated exams.

METHODOLOGY

The study, designed as a cross-sectional investigation, was carried out in the Department of Ophthalmology at Hayatabad Medical Complex, Peshawar after approval from the Hospital Research and Ethical Committee (IREB). It aimed at assessing retinal nerve fiber layer (RNFL) thinning in patients newly diagnosed with primary open-angle glaucoma (POAG). The sample comprised of 136 eyes, determined using a 14.9% prevalence rate for RNFL thinning in early glaucoma, with a margin of error set at 6% and a 95% confidence interval, calculated via the WHO formula. A consecutive, non-probability sampling method was employed during the study period from 1st May, 2021 to 31st March, 2022.

During selection of patients, the following inclusion criteria was followed: individuals newly diagnosed with POAG, aged between 30 and 70 years, from either gender. Exclusion criteria were established to mitigate potential confounders that could distort RNFL thickness analysis, including any glaucoma diagnosis other than POAG, a history of corneal refractive or intraocular surgery (excluding uncomplicated cataract surgery), posterior segment diseases (such as diabetic retinopathy, and retinal vascular diseases), and a refractive error exceeding ± 4.00 D Spherical equivalent. The data collection process commenced following synopsis approval, with patients presenting to the glaucoma clinic undergoing thorough ophthalmic examinations. Subjects meeting the eligibility criteria were included in the study after providing informed consent. RNFL thickness was measured using OCT (Spectralis, Heidelberg, Germany), focusing on global-RNFL (G-RNFL) thickness, with scans accepted based on manufacturer recommendations. In instances of bilateral POAG, the eye with worse G-RNFL thickness was selected, or the right eye if both were equal.

Data analysis was performed using SPSS version 24, with mean ± SD calculated for continuous variables such as age, BCVA, IOP at presentation, and G-RNFL thickness. RNFL thickness was further stratified by age and gender to explore effect modification, employing ANOVA for age group comparisons, and t-tests for RNFL thinning, with a significance level set at $p < 0.05$.

RESULTS

The study was conducted on 136 patients with POAG. The mean age of the study sample was 54.5 ± 13.6 years. Most of the patients (52.2%) were in the age group 55–80 years, and when considering gender distribution, there were 66.9% males and 33.1% females. Additionally, the mean duration of POAG was 239.2 ± 106.1 days, with most patients (65.4%) presenting within 180–360 days.

Table -1: Demographics and Clinical Characteristics of POAG Patients.

Age Group	
15 - 35 years	12 (8.8%)
>35 - 55 years	53 (39.0%)
>55 - 80 years	71 (52.2%)
Gender	
Male	91 (66.9%)
Female	45 (33.1%)
Duration of POAG	
Upto - 90 days	16 (11.8%)
> 90 - 180 days	31 (22.8%)
> 180- 360 days	89 (65.4%)

Regarding clinical measurements, most patients had a mean BCVA of 0.8 ± 0.77, which was statistically insignificant with a p-value of 0.143. Similarly, the mean IOP of 18.9 ± 9.1 mmHg showed no statistical significance with a p-value of 0.190.

Table -2. Clinical Measurements by Age Group

Age Group	BCVA Mean (SD)	IOP Mean (SD)	G-RNFL Thickness Mean (SD)	P- Value (BCVA/ IOP/ GRNFL)
15-35 years	0.633 (0.311)	22.42 (11.84)	71.33 (31.65)	0.143
>35-55 years	0.564 (0.593)	19.79 (9.99)	62.19 (19.14)	0.190
>55-80 years	0.806 (0.775)	17.80 (7.71)	66.80 (22.60)	0.329

One way ANOVA was applied. P Value less than 0.05 was taken as significant.

Table - 3. G-RNFL Thickness by Duration of POAG

Duration of POAG	G-RNFL Thickness Mean (SD)	P- Value
Up to 90 days	65.63 (17.79)	
> 90-180 days	65.94 (22.89)	0.986
> 180-360 days	65.18 (22.97)	

Independent t test was applied. P value less than 0.05 was taken as significant.

DISCUSSION

Retinal Nerve Fiber Layer (RNFL) thickness has been linked to visual acuity as well as patient demographics like age, gender, and race. In healthy subjects and glaucoma-suspect individuals, there was a strong inverse association between increasing age and decreasing thickness. Firatli et al investigated the difference in change in the RNFL and Ganglion cell complex (GCC) thickness with age and found that the amount of decrease was more in healthy individuals.[9] Thus age is an important modifier of the relationship between IOP and glaucomatous loss of RNFL thickness with older patients more susceptible to visual morbidity.[10] Studies on RNFL thickness between males and females have found significant differences with thickness more in males.[11] Similarly association with race has also been demonstrated in several studies.[12] In one study it was observed that Caucasians tend to have thinner RNFL thickness compared to Hispanics and Asians while in another mean global RNFL thickness was slightly greater among black participants compare to Indian participants.[13]

In addition to demographics, the different refractive states like myopia, hyperopia and astigmatism also have a proven significant effect on the RNFL thickness. Myopic eyes tend to have a thinner RNFL thickness compared to emmetropic eyes.[14] Also there was an inverse correlation with higher degrees of myopia resulting in thinner RNFL. Similarly hyperopic eyes had a thicker RNFL compared to emmetropic eyes.[15] The mechanism behind these associations is still not completely cleared. Different pathological states also affect the RNFL thickness. Yekta et al. found inverse correlation between mean RNFL thickness and contrast sensitivity in patients diagnosed with Optic Neuritis.[16]

In their study, Zou et al. established a correlation between the thickness of the inner nuclear layer (INL) across foveal, parafoveal, and perifoveal regions and visual acuity in patients diagnosed with

idiopathic epiretinal membrane (ERM).[17] Similarly, Parrozzani et al. reported a significant reduction in the mean retinal nerve fiber layer (RNFL) thickness in the peripapillary region in pediatric patients presenting with optic pathway glioma (OPG).[18] In a separate investigation, Bozali and Yalinbas identified a noteworthy decrease in RNFL thickness within the inferior and superior quadrants among patients with schizophrenia, potentially indicating a connection to visual acuity alterations.[19] Furthermore, Ayaki et al. observed a positive relationship between eye fatigue and the thickness of the macular ganglion cell complex (GCC), suggesting that non-visual symptoms might be associated with changes in visual acuity.[20]

Contemporary research has highlighted the variability of RNFL thickness among different populations and even within the same population by shedding light on confounding variables even in individuals with no glaucoma, suggesting the importance of individual baseline measurements. Our results contribute to this discussion by providing data on RNFL thickness in a specific population in which no solid trends could be identified; the mean RNFL thickness was less in the 35-55 population compared to the 15-35 population however it was more than the 55–80-year population. Another interpretation could be that RNFL thickness may not differ significantly in the early stages of disease and stratification can only be identified in more advanced stages of the disease.

The early diagnosis of Primary Open angle glaucoma (POAG) remains difficult specially in non-tertiary centers in developing countries with no access to OCT and poor patient follow-up. Although our study did not find statistically significant differences in RNFL thickness between early and advanced glaucoma patients; the predictive value of the OCT remains and highlights the need for more thorough longitudinal studies to understand the early changes in RNFL thickness and what their clinical implications are.

Limitations of our study include the lack of confounding factors incorporated into analyzing the RNFL thickness and the sample including only a single race. Future studies should take this into account and the RNFL thickness should be analyzed quadrant wise and at multiple points in time to make our understanding of the conundrum that is Glaucoma.

Conclusion

The measurement of RNFL thickness will retain its crucial role in the diagnosis and management of POAG (and other neuropathies). Our study contributes to the ongoing discussion about the variability of RNFL thickness and its implications for clinical practice. By focusing on a specific patient population, we provide a basis for future research aimed at improving visual outcomes in patients with POAG.

Conflict of Interest: None to declare

Ethical Approval: The study was approved by the Institutional Review Board / Ethical Review Board Vide No.331/HEC/B&PSC/2020.

Author Contributions: Sundas Gul: Concept, Design, Data Collection.

Bakht Danyal Khan: Data Collection, Literature Search, Article Draft.

Yousaf Jamal Mahsood: Data Analysis, Critical Review.

REFERENCES

1. Faiq MA, Sofi RA. A glimpse into the mysteries of glaucoma: From theories to clinics. Oman J Ophthalmol. 2019;12(1):1. doi:10.4103/ojo. OJO_91_2018.

2. Allison K, Patel D, Alabi O. Epidemiology of glaucoma: the past, present, and predictions for the future. Cureus. 2020;12(11). doi:10. 7759/ cureus.11686.

3. Steinmetz JD, Bourne RRA, Briant PS, Flaxman SR, Taylor HRB, Jonas JB, et al. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. Lancet Glob Health. 2021;9(2):e144–60. DOI:10.1016/S22

14-109X(20)30489-7.

4. Hassan B, Ahmed R, Li B, Noor A, Hassan Z ul. A comprehensive study capturing vision loss burden in Pakistan (1990-2025): Findings from the Global Burden of Disease (GBD) 2017 study. PloS One. 2019;14(5):e0216492. https://doi.org/10.1371/journal.phone.0216492.

5. Leske MC, Heijl A, Hyman L, Bengtsson B. Early Manifest Glaucoma Trial: design and baseline data. Ophthalmology. 1999;106(11):2144–53. DOI:10.10161/s0161-6420(99)90497-9.

6. Tatham AJ, Weinreb RN, Medeiros FA. Strategies for improving early detection of glaucoma: the combined structure & ndash; function index. Clin Ophthalmol. 2014;8:611–21. DOI:102147/ OPTH.S44586.

7. Hood DC, La Bruna S, Tsamis E, Thakoor KA, Rai A, Leshno A, et al. Detecting glaucoma with only OCT: Implications for the clinic, research, screening, and AI development. Prog Retin Eye Res.2022;90:101052.DOI:10.1016/jpretey eres.2022.101052.

8. Chen TC, Hoguet A, Junk AK, Nouri-Mahdavi K, Radhakrishnan S, Takusagawa HL, et al. Spectral-Domain OCT: Helping the Clinician Diagnose Glaucoma: A Report by the American Academy of Ophthalmology. Ophthalmology. 2018;125(11):1817–27. DOI:10.1016/j.ophtha.2018.05.008.

9. Firatli G, Elibol A, Altinbas E, Ayhan C, Celebi ARC. The Comparison of Age-related Change in Retinal Nerve Fiber Layer and Ganglion Cell Complex Thicknesses between Glaucoma Suspects and Healthy Individuals. J Curr Glaucoma Pract. 2023;17(1):22-29. doi:10.5005/jp-journals-10078-1392.

10. Jammal AA, Berchuck SI, Thompson AC, Costa VP, Medeiros FA. The Effect of Age on Increasing Susceptibility to Retinal Nerve Fiber Layer Loss in Glaucoma. Invest Ophthalmol Vis Sci.2020;61(13):8. doi:10.1167/iovs.61.13.8.

11. Chueh KM, Hsieh YT, Chen HH, Ma IH, Huang SL. Identification of sex and age from macular optical coherence tomography and feature analysis using deep learning. Am J Ophthalmol. 2022;235:221-228.doi:10.1016/j.ajo.2021.09.015.

12. Alasil Tarek, Wang Kaidi, Keane Pearse A, Lee Hang, Baniasadi Neda, de Boer, et al. Analysis of Normal Retinal Nerve Fiber Layer Thickness by Age, Sex, and Race Using Spectral Domain Optical Coherence Tomography. J Glaucoma. 2013;22(7):532-541. DOI:10.1097/IJG.0b013e318255bb4a.

13. Murugan C, Golodza BZ, Pillay K, Mthembu BN, Singh P, Maseko SK, et al. Retinal nerve fibre layer thickness of black and Indian myopic students at the University of KwaZulu-Natal. Afr Vis Eye Health 2015;74:6. https://doi.org/10.4102/aveh.v74i1.24.

14. Negm Eldin H. Abd Allah. LSE, HAZEM M.O. MOHAMED RASHED, ALSHIMAA A.S. ELSROUGY. Evaluation of the Relationship between Retinal Nerve Fibres Layer (RNFL) Thickness in Myopia versus Hypermetropia. The Med J Cairo Uni. 2021;89:1651–8. https://doi.org/10.21608/mjcu.2021.194981.

15. Qian Y, Ma Y, Lin Q, Xiang Z, Qiang J, Xu Y, et al. Retinal and Choroidal Changes in Children with Moderate-to-High Hyperopia. J Ophthalmol. 2021;2021:9971564. doi:10.1155/2021/9971564.

16. Yekta AA, Sorouh S, Asharlous A, Mirzajani A, Jafarzadehpur E, Soltan Sanjari M, et al. Is retinal nerve fibre layer thickness correlated with visual function in individuals having optic neuritis? Clin Exp Optom. 2022;105(7):726-732. doi: 10.1080/08164622.2021.1969213.

17. Zou J, Tan W, Huang W, Liu K, Li F, Xu H. Association between individual retinal layer thickness and visual acuity in patients with epiretinal membrane: a pilot study. Peer J. 2020;8:e9481. doi:10.7717/peerj.9481.

18. Parrozzani R, Miglionico G, Leonardi F, Pulze S, Trevisson E, Clementi M, et al. Correlation of peripapillary retinal nerve fibre layer thickness with visual acuity in paediatric patients affected by optic pathway glioma. Acta Ophthalmol.

2018;96(8):e1004-e1009. doi: 10.1111/aos. 13803.

19. Bozali E, Yalinbas D. Analysis of the Thickness of the Outer Retinal Layer Using Optical Coherence Tomography - A Predictor of Visual Acuity in Schizophrenia. Analyse der äußeren Netzhautschichtdicke als Prädiktor der Sehschärfe mittels optischer Kohärenztomografie bei Schizophrenie. Klin Monbl Augenheilkd. 2022;239(10):1232-1238. doi:10.1055/a-1741-7988.

20. Ayaki M, Kuze M, Kondo M, Tsubota K, Negishi K. Association between Retinal Nerve Fiber Layer Thickness and Eye Fatigue. Biomed Res Int. 2019;2019:3014567. doi:10. 1155/2019/301456.