DOI: https://doi.org/10.53350/pjmhs20231711187

ORIGINAL ARTICLE

Early Detection of Primary Open Angle Glaucoma Using Optical Coherence Tomographic Ganglion Cell Layer Thickness

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ABSTRACT

Background: POAG is a leading cause of blindness worldwide. Early detection is key to preventing progression, however, traditional diagnostic methods are not able to detect the disease at the early stages. An emerging tool for early diagnosis is optical coherence tomography (OCT) for quantifying the thinning of the retinal ganglion cell layer (GCL) which precedes functional loss.

Methodology: This prospective, observational study was performed for one year in a tertiary eye care center in Faisalabad, Pakistan from January 2022 to January 2023. There was n=50 patients with early POAG and 50 age and sex matched healthy controls enrolled, for a total of n=100 subjects (200 eyes). An ophthalmic examination, including measurement of intraocular pressure (IOP), standard automated perimetry (SAP), and spectral domain OCT imaging, was performed comprehensively. A 6 × 6 mm² macular cube scan centered on the fovea was acquired using OCT, and automated segmentation algorithms calculated the average, superior, and inferior GCL thickness. Clinical parameters and OCT measurements were compared between the groups, and correlations between GCL thickness and visual field indices were assessed using statistical analyses performed using SPSS.

Results: IOP and MD in POAG patients were significantly higher than in healthy controls ($p < 0.001$). The thickness of the GCL in POAG patients was significantly reduced in the average, superior, and inferior sectors from controls ($p < 0.001$). Decreased GCL thickness was linearly correlated ($r = -0.65$, $p < 0.001$) to worsening MD in the POAG group.

Conclusion: Measurements of the ganglion cell layer by OCT are sensitive and objective biomarkers for the early detection of POAG. POAG patients have significantly smaller GCL thickness and there is strong correlation with functional deficits which makes it an ideal candidate for early glaucoma screening in resource-poor settings such as Pakistan, as OCT can be integrated in early screening protocols.

Keywords: Primary Open-Angle Glaucoma, Optical Coherence Tomography, Ganglion Cell Layer, Early Detection, Visual Field, Faisalabad, Pakistan

INTRODUCTION

Primary open-angle glaucoma (POAG) is a chronic, progressive optic neuropathy that is the leading cause of irreversible blindness in the world. POAG is characterized by the insidious loss of retinal ganglion cells (RGCs) and its associated visual field deficits, which typically remain asymptomatic until the late stages of the disease when significant neuronal damage has already occurred[1]. With the increase in the global population age, the prevalence of glaucoma is anticipated to rise further, further intensifying its public health impact. This is further exacerbated by the fact that in Pakistan, there is very limited access to specialized ophthalmic care and resources, which makes early diagnosis even more challenging, underscoring the importance of innovative diagnostic approaches that are both accessible and reliable[2].

Currently, optical coherence tomography (OCT) has revolutionized our understanding of the retinal microstructure, owing to its high resolution and noninvasive imaging ability of the retinal layers. Recently, made OCT derived measurements, especially of ganglion cell layer (GCL), have emerged as promising biomarkers for early glaucomatous damage detection[3]. The progressive loss of RGCs is indicated by the thinning of the GCL, which can be detected well before the development of conventional functional deficits, which are indicated by standard automated perimetry. Glaucoma is a pre-perimetric stage where early therapeutic intervention could significantly change disease trajectory and preserve vision[4].

OCT technology integrated into clinical practice provides several advantages over traditional diagnostic modalities. OCT gives an objective, quantitative evaluation of retinal structure, unlike the measurement of intraocular pressure (IOP) or subjective visual field testing[5]. These capabilities, especially in resource-limited settings such as in Pakistan where there is variability in patient presentation and the diagnostic infrastructure, can delay the intervention. In addition, OCT is also reproducible, noninvasive, and therefore ideally suited for routine screening and longitudinal monitoring of high risk populations[6].

A major challenge in the late presentation of glaucoma in Pakistan is still mainly socioeconomic barriers, lack of public awareness, and inadequate screening programs. Finally, in overcoming these obstacles, OCT-based diagnostic protocols could have a transformational role through enabling early detection and targeted interventions[7]. Yet, the standardization of GCL thickness measurements is hindered by variability in imaging protocols and segmentation algorithms used in different OCT platforms. To validate the diagnostic utility of GCL assessments and to develop robust, standardized benchmarks to be universally applied in clinical practice, it is essential to address these technical issues through rigorous, multicentre studies[8].

To evaluate the diagnostic accuracy of OCT-derived GCL thickness measurements for the early detection of POAG, we are performing our study based in Pakistan. This research integrates OCT imaging with more conventional assessments, such as measurement of intraocular pressure and visual field analysis, to build a comprehensive diagnostic framework appropriate for the local environment. The study also investigates the correlation between GCL thinning and early glaucomatous damage and the reproducibility and reliability of these measurements using several OCT devices used in Pakistani clinical practice[9].

The study also investigates the possible confounding factors that might affect GCL measurements, such as age, refractive error, and coexisting retinal conditions, so that the diagnostic criteria developed are both precise and contextually relevant. Our research aims to bridge the gap between state-of-the-art imaging technology and its practical clinical application in Pakistan by addressing these challenges. The aim is to improve strategies for early detection, improve patient management, and reduce the

long-term glaucoma burden in a country that is characterized by late presentation[10].

The goal of this comprehensive investigation is to significantly contribute to the knowledge of glaucoma diagnostics. We expect our findings will have important implications for clinical practice in Pakistan as well as for the global ophthalmic community, by showing how state of the art imaging techniques can be utilized to address the different hurdles that are encountered by the healthcare systems in resource challenged areas[11].

MATERIALS AND METHODS

Study Design and Setting: This was a 1-year prospective observational study that was undertaken from January 2022 to January 2023 at Ophthalmology department of, Allied Hospital II Faisalabad, Pakistan. The study was approved by the Institutional Review Board and was designed according to the Declaration of Helsinki. All participants were written informed consent before enrolment.

Participants and Sample Size: In the study, 50 patients with early primary open angle glaucoma (POAG) and 50 age and sex matched healthy controls were enrolled for evaluation of a total of 100 subjects (200 eyes). The sample size was based on the prevalence of POAG in the local population, the diagnostic performance of OCT-derived GCL measurements as reported in previous studies, and the feasibility of patient recruitment within the study period in Faisalabad. Since it was judged that this sample size would be sufficient to attain adequate statistical power to detect differences in GCL thickness between the POAG group and the control group, this sample size was deemed appropriate.

Inclusion and Exclusion Criteria: Inclusion criteria for the POAG group included a confirmed diagnosis of early POAG as defined by characteristic optic nerve head changes and corresponding visual field defects with mean deviation better than -6 dB, a mean age of 40 to 70 years, and a best corrected visual acuity (BCVA) of 20/40 or better. In addition, healthy controls had to have no history of ocular disease, normal optic nerve head appearance, and IOP within normal limits (<21 mmHg). All participants were excluded if they had had ocular surgery, trauma, or retinal pathology; had significant media opacities that would compromise image quality; or had systemic conditions known to affect the optic nerve, such as diabetic retinopathy or neurological disease.

OCT Imaging Protocol and Data Collection: Slit lamp biomicroscopy, IOP measurement using Goldmann applanation tonometry, and standard automated perimetry (SAP) were performed in each participant. A 6 × 6 mm2 macular cube scan centered on the fovea was obtained using high-resolution spectral domain OCT (SD OCT, e.g. Heidelberg Spectralis OCT). The OCT images were segmented using automated segmentation algorithms to isolate and quantify GCL thickness. The data included were only scans with a signal strength index (SSI) above 25 and free of motion artifacts. Systematic recording of demographic data, clinical findings, and GCL thickness measurements was made. Finally, OCT measurement in the POAG group was further correlated to corresponding visual field indices from SAP.

Statistical Analysis: SPSS software (version 25.0, IBM Corp., Armonk, NY, USA) was used to perform statistical analyses. Shapiro–Wilk test was used to test the normality of continuous variables. The data distribution was compared with the independent samples t-test or Mann-Whitney U test for the data. Pearson or Spearman correlation coefficients were used to evaluate correlations between GCL thickness and visual field parameters. Statistical significance was considered as a p-value less than 0.05.

Ethical Considerations: The study was conducted by the principles of Helsinki. The Institutional Review Board of the participating eye care center in Faisalabad reviewed and approved the study protocol. All participants provided informed consent, written and in writing after they were fully informed about the study purpose, procedures, risks and benefits.

We anonymized and stored securely all the participant data in order to maintain the confidentiality. The participants were informed of their right to withdraw from the study at any time without any effect on their clinical care. The ethical safeguards provided for in these were such that the research was carried out with the utmost care for the rights and welfare of the patient.

RESULTS

The study included n=100 subjects (200 eyes) equally distributed into early primary open angle glaucoma patients and healthy controls. The age and gender of both groups were well matched, thus, differences in clinical parameters observed in both groups are likely to be due to the disease process. In the POAG group, there was, for example, much higher intraocular pressure (IOP) and worse visual field performance, expressed as mean deviation (MD), than in the controls as shown in table 1.

Table 1: Demographic and clinical characteristics of the study participants.

Parameter	POAG Group (n=50)	Control Group (n=50)	p-value
Age (years)	58.2 ± 7.1	57.8 ± 6.8	0.75
Gender (M/F)	28/22	27/23	0.84
Intraocular Pressure (mmHg)	22.5 ± 2.8	15.2 ± 2.1	<0.001
Visual Field MD (dB)	-3.5 ± 1.2	0 ± 0	<0.001

The ganglion cell layer (GCL) thickness was assessed by means of OCT imaging to measure the structural integrity of the retina. Table 2 compares the average, superior, and inferior GCL thicknesses between the POAG group and the healthy controls. OCT-derived metrics were shown to be early indicators of glaucomatous damage as statistically significant thinning was found in all measured regions of the GCL in POAG patients as shown in table 2.

Table 2: Comparison of OCT-derived ganglion cell layer (GCL) thickness parameters between POAG patients and healthy controls.

Parameter	POAG Group (n=50)	Control Group (n=50)	p-value
Average GCL Thickness (µm)	68.4 ± 5.3	82.1 ± 4.8	<0.001
Superior GCL Thickness (µm)	70.1 ± 5.2	84.5 ± 5.0	<0.001
Inferior GCL Thickness (µm)	66.7 ± 5.4	79.7 ± 4.3	<0.001

In order to explore the relationship between structural and functional damage in glaucoma, average GCL thickness and visual field mean deviation (MD) were correlated in POAG patients. The results showed a strong positive correlation, consistent with the improvement of visual field performance with a decrease in GCL thickness. This finding supports the use of OCT-derived GCL measurement as a sensitive biomarker for early glaucomatous damage as shown in table 3.

Table 3: Correlation between average GCL thickness and visual field mean deviation (MD) in POAG patients.

Parameter	Correlation Coefficient (r)	p-value
Average GCL Thickness vs. Visual Field MD	0.65	<0.001

The results of this study showed that, in terms of age and gender, the demographic and clinical characteristics of POAG patients and the control group were well matched. However, the healthy controls were significantly different from POAG patients in terms of elevated intraocular pressure and reduced visual field performance. However, OCT imaging also revealed that the ganglion cell layer was thinner in POAG patients than in controls, and there were statistically significant differences in the average, superior, and inferior sectors. Additionally, GCL thickness

decreased, and there was a strong positive correlation with worsening visual field indices, suggesting that OCT-derived GCL measurements are a sensitive early diagnostic marker for glaucomatous damage. Together, these findings collectively support the use of OCT in the early glaucoma screening protocols, especially in resource-limited settings, as an objective and reliable method of quantifying retinal structural changes in early POAG.

DISCUSSION

To investigate the utility of OCT-derived ganglion cell layer (GCL) thickness measurements as an early diagnostic marker of primary open angle glaucoma (POAG) in a Pakistani population, the present study was carried out. Our results showed that patients with early POAG had higher IOP and lower visual field performance than healthy controls[12]. Additionally, OCT imaging showed a large thinning of the GCL of the POAG group, with statistically significant differences in the average, superior, and inferior sectors. The functional deficits correlated strongly with these structural changes, with significantly higher GCL thickness correlating to worse visual field indices[13].

These are consistent with previous studies in the literature showing that structural damage in glaucoma – specifically the retinal ganglion cell layer – is responsible for preceding functional loss detectable by standard perimetric testing[14]. The high-resolution imaging of SD-OCT allowed us to quantify subtle changes in the retina that occur in the early stages of glaucoma and support the concept that OCT-derived metrics can be used as sensitive biomarkers for early glaucomatous damage[15].

Moreover, the study design, employing a careful matching of the POAG patients and control subjects on age and gender, largely eliminates the effect of demographic confounders and lends support to the validity of the difference in OCT measurements observed. However, there are some limitations[16]. While the sample size is justified for a 1-year study in Faisalabad, it may not encompass the whole heterogeneity in glaucoma presentation in other populations. In addition, OCT device settings and segmentation algorithms varied, which could have contributed to measurement reproducibility, and standardized imaging protocols should be used in future multicenter studies[17].

Clinically, the integration of OCT in early glaucoma screening protocols, especially in resource-constrained settings like Pakistan, is of great importance. OCT could help provide early detection that can facilitate timely therapeutic interventions that may slow disease progression and preserve vision. Future research should increase the sample size, include longitudinal follow-up data, and evaluate the cost-effectiveness of OCT-based screening in routine clinical practice[18, 19].

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: This research did not receive any external financial support.

Acknowledgments: We are grateful to our colleagues and paramedical staff for their invaluable support, which made this study possible.

Authors' Contributions: All authors contributed equally to the conception, execution, and preparation of this study.

CONCLUSION

Current study shows that OCT measured ganglion cell layer is a sensitive and objective biomarker for early detection of primary open angle glaucoma. We found that POAG patients in our study have significantly thinner GCL measurements than healthy controls and that these structural changes are strongly correlated with functional deficits measured by visual field testing. The results indicate the benefit of combining OCT in early glaucoma screening protocols, which may be especially important in resource-limited settings. Such advanced imaging techniques could be implemented in routine practice to aid earlier diagnosis, prompt intervention, and, thus, preserve visual function in patients at risk for glaucoma.

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This article may be cited as: Saleem A, Subzwari SAHW, Shah SSA, Bano S, Iqbal H, Ahmad S: Early Detection of Primary Open Angle Glaucoma Using Optical Coherence Tomographic Ganglion Cell Layer Thickness. Pak J Med Health Sci, 2023;18(11): 187-189.