DOI: https://doi.org/10.54393/pjhs.v6i5.3035

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 05 (May 2025)

Original Article

OPEN ACCESS

Evaluation of Variability in Macular Thickness in Primary Open Angle Glaucoma: A Spectral Domain Optical Coherence Tomography-Based Study

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ARTICLE INFO

Keywords:
Glaucoma, Macular Thickness, Spectral Domain Optical Coherence Tomography, Primary Open-Angle Glaucoma

How to Cite:
Tanveer, T., Ali, M., Akram, F., Sughra, U., Anwar, A., & Khan, F. (2025). Evaluation of Variability in Macular Thickness in Primary Open Angle Glaucoma: A Spectral Domain Optical Coherence Tomography-Based Study: Primary Open Angle Glaucoma: A Spectral Domain Optical Coherence Tomography-Based Study.Pakistan Journal of Health Sciences, 6(5),182-186. https://doi.org/10.54393/pjhs.v6i5.3035

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Received Date: 8th April, 2025
Revised Date: 19th May, 2025
Acceptance Date: 26th May, 2025
Published Date: 31st May, 2025

ABSTRACT

Globally, glaucoma, especially primary open-angle glaucoma (POAG), is one of the leading causes of blindness. This disease is connected to damage of the optic nerve head, death of retinal ganglion cells and visual field abnormalities. **Objectives:** To check the macular thickness and total macular volume using spectral-domain optical coherence tomography (SD-OCT) among patients of POAG and subjects without glaucoma. **Methods:** The observational case-control study, where 40 participants had POAG and 40 participants the same age did not. Only the right eye or only the left eye from each subject was examined in the study. All subjects had a thorough check of their eyes which included history, eye chart testing, slit-lamp examination, dilated fundus inspection, gonioscopy and measuring intraocular pressure (IOP). Visual fields were assessed using the Humphrey Field Analyzer. Macular thickness (MT) was analyzed with SD-OCT using OCT Spectralis. Parameters evaluated were macular inner thickness (MIT), macular outer thickness (MOT), macular central thickness (MCT) and macular total volume (MTV). **Results:** Patients with POAG exhibited markedly reduced MTV, MIT and MOT in comparison to healthy controls, with the greatest decline observed in the temporal as well as the inferior quadrants. These observations confirm that structural differences in the macular parameters are correlated with glaucoma and can aid in early diagnosis and monitoring progression. **Conclusion:** This study emphasizes the diagnostic utility of SD-OCT in determining macular thickness variability in individuals with POAG. Our findings show that macular thickness is much lower in glaucomatous eyes than in healthy controls, with distinct patterns of regional thinning indicating retinal ganglion cell vulnerability.

INTRODUCTION

When a person has glaucoma, the retinal ganglion cells (RGCs) and their axons are damaged, which results in damage to the optic nerve and certain kinds of visual field problems [1, 2]. It is well-known around the globe as one of the main causes of permanent vision problems [3]. To manage the disease and save vision, it's very important to identify it early and watch it closely [2, 4]. Glaucoma is clinically recognized by checking for damage to the optic nerve head and measuring visual field defects. Using standard perimetry, abnormalities in the visual field are found only after much of the retinal nerve fiber layer (RNFL) is affected [5]. Appropriate diagnosis of glaucomatous damage in the early stages helps save sight. Because of this, testing the retinal nerve fiber layer and the retinal ganglion cell layer helps find glaucoma at an early stage [6]. Examining the macula is interesting because it contains a big group of retinal ganglion cells, many of which are affected in the early stages of glaucoma. The macular area has 4–6 layers containing ganglion cells, which make up about 30–35% of its total thickness. For this reason, damage to macular ganglion cells causes the retinal nerve fiber layer to become much thinner [7]. There is a strong connection between RNFL thinning, reduced vision fields, changes in macular thickness and reduced ganglion cell

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density, which means looking at the macula can provide important information about the early stages of glaucoma [8, 9]. SD-OCT is now used regularly to capture detailed cross-sectional images of the retina. By using SD-OCT, you can identify inner retinal and macular thickening, which makes it valuable for diagnosing the early effects of glaucoma, especially when there is little to no thinning around the optic nerve [10]. POAG causing changes in the macular area has attracted more attention because studies suggest that early glaucomatous change may take place in the macula and lead to problems with central vision. At the moment, it is not understood why there can be significant differences in macular thickness within glaucomatous eyes. This variability is necessary for us to detect health problems, observe changes in the condition and decide what care should include. Based on what we saw in the reviewed research, we proposed that SD-OCT values for macular thickness are the same in eyes with primary open-angle glaucoma as in those of similarly-aged healthy people. These metrics measured with SD-OCT can play a big role in detecting early changes in the macula of glaucoma patients and may be used for diagnosis and tracking of POAG.

This study aims to evaluate region-specific macular thinning in POAG eyes compared to healthy individuals. Macular central thickness (MCT), macular inner thickness (MIT), macular outer thickness (MOT), and macular total volume (MTV) in POAG patients are compared to healthy individuals.

METHODS

This observational case-control study was carried out at the Al-Shifa Trust Eye Hospital (ASTEH), Rawalpindi, Pakistan, from May 15th, 2024, to December 30th,2024, using non-probability consecutive sampling. It included 80 participants segregated into two categories: Group 1 consisted of 40 individuals diagnosed with POAG, while Group 2 comprised 40 healthy control subjects. Ethical approval was obtained from the institute's Ethical Review Committee on May 3, 2024 (approval number: ERC-17/AST-24). Before enrollment, all participants provided informed consent following detailed counselling about the study. The study adhered to the principles of the Declaration of Helsinki. Patients included in the study were referred to the Glaucoma Department from the General OPD (Outpatient Department). The diagnosis of POAG in Group-1 was made on intraocular pressure (IOP) measurements of more than 21mm of Hg on Goldman applanation tonometer on at least 3 occasions, presence of glaucomatous optic nerve head changes (a cup-disc ratio (CDR) exceeding 0.4 or an inter-eye CDR disparity greater than 0.2), and detection of characteristic visual field defects using the Humphrey Visual Field Analyzer (Carl Zeiss). Each patient exhibited loss of visual fields (mean deviation >6dB) in at least two successive automated perimetric examinations. Gonioscopy was done utilizing Posner 4-mirror goniolens which verified open anterior chamber angles (Shaffer grades 3 or 4) and the exclusion of secondary glaucoma or non-glaucomatous optic neuropathy. In contrast, participants in Group 2, which included the healthy participants, displayed no signs or symptoms of glaucoma, had no relevant ocular history, and had no retinal diseases. Their IOP measurements on the Goldman applanation tonometer were all below 21 mmHg on more than 2 occasions, and no abnormalities were observed in their optic nerve heads or visual fields. Exclusion criteria included subjects with a history of ocular surgery or trauma, lenticular opacities, diabetic retinopathy, macular dystrophy or degeneration, epiretinal membrane, macular edema, retinal detachment, non-glaucomatous optic nerve diseases, or spherical equivalent refractive error larger than ± 6 diopters. Open-Source Epidemiologic Statistics for Public Health, Version 3.01 [11] was used to calculate how many cases in each group should be included to allow statistical comparison. The reference study by Sharma *et al.*, [10] shows, using a statistical power of 95%, significance of 0.05 and a 95% confidence interval, that the sample size required for the mean outer macular thickness was determined as 15 participants for each group. As a way to get a better estimate with some discrepancy in data accounted for, the groups were set at 40, giving a total of 80 participating individuals. All the participants were examined which involved taking down their history, confirming eyesight using the Snellen visual acuity chart, checking the eye on a slit lamp and seeing the back of the eye with a fundoscope. More assessment steps were performed with the 4-mirror goniolens for gonioscopy, and pressured IOP was measured using Goldmann Applanation Tonometry. To perform the dilated fundus examination, a +90-diopter lens was used, and perimetry was completed with the Humphrey Visual Field Analyzer (Carl Zeiss, USA). The thickness of the macula was evaluated in all patients with SD-OCT, using the OCT Spectralis (Heidelberg Engineering, Inc., Germany), by only one trained person. Macular inner thickness (MIT) was measured within the innermost 3 mm of the retina, outer macular thickness (MOT) in the region between 3 mm and 6 mm and total macular volume (MTV) was also measured. IBM SPSS Statistics version 26.0 on Windows was chosen for data analysis. To make sure continuous variables are normally distributed, the Shapiro-Wilk test was applied ahead of parametric tests. The independent t-test method was chosen to check if the given mean differences can be seen for normally distributed data. Mean plus or minus SD was used to show quantitative data. A p-value of less than 0.05 was considered statistically significant for all tests.

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RESULTS

Muscular thickness map is shown in Figure 1.

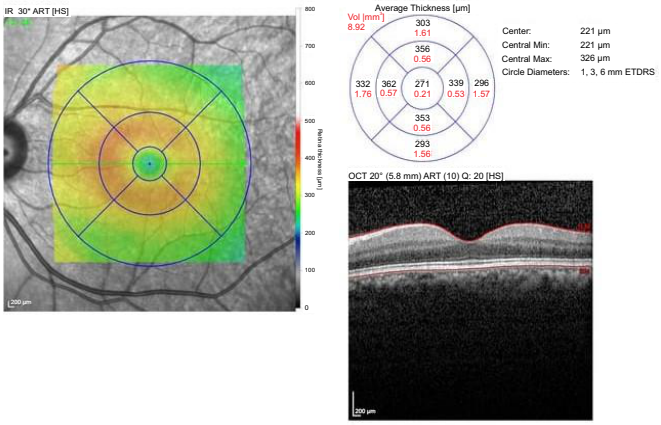

Figure 1: Macular Thickness Map

In total, 80 subjects were inducted in the study, with 40 individuals identified as POAG forming Group-1 and 40 disease-free individuals comprising Group-2. There was no remarkable age disparity between the two groups (p=0.019); nevertheless, the male-to-female ratio differed slightly, with Group-1 showing a nearly equal distribution (21:20) compared to Group-2 (19:22). The mean intraocular pressure (IOP) was notably elevated in Group-1 (17.98 mmHg) compared to Group-2 (14.37 mmHg, p<0.0001). Additionally, the cup-to-disc (CD) ratio was markedly increased in Group 1 (0.6) as compared to subjects in Group 2 (0.2, p<0.0001), emphasizing the structural differences associated with glaucoma (Table 1).

Table 1: Baseline Demographic and Clinical Features of the Subjects

Demographic Features	Group 1 (n=40)	Group 2 (n=40)	p-Value
Age (Years)	54.83	50.28	0.019
Male: Female Patient Ratio	20:20	19:21	0.5
Cup Disc Ratio	0.62	0.26	<0.0001
Mean IOP (mmHg)	17.98	14.45	<0.0001

Analysis of the OCT macular thickness map demonstrated a significant decline in both inner and outer thickness of the macula across all quadrants in patients with diagnosed POAG compared to healthy controls. For macular inner thickness (MIT), Group-1 exhibited significantly lower values in the temporal (309.76 ± 21.05 µm vs. 319.56 ± 16.76 µm, p=0.022, Cohen's d=0.52), superior (319.37 ± 25.59 µm vs. 332.32 ± 18.76 µm, p=0.011, Cohen's d=0.58), nasal (321.27 ± 26.88 µm vs. 333.59 ± 18.34 µm, p=0.018, Cohen's d=0.54), and inferior quadrants (315.1 ± 24.39 µm vs. 330.2 ± 17.33 µm, p=0.002, Cohen's d=0.73) (Table 2).

Table 2: Macular Inner Thickness (MIT) Across All Quadrants

Variables	Group 1, POAG (n=40)	Group 2, Controls (n=40)	p-value	Mean Difference	95%CI Lower Limit	95%CI Upper Limit	Effect Size Cohen's d
	Mean (µm) ± SD (µm)						
Temporal	309.30 ± 21.10	319.43 ± 16.95	0.020	-10.12	-18.64	-1.60	0.52
Superior	318.90 ± 25.74	332.20 ± 18.90	0.010	-13-30	-23.35	-3.24	0.58
Nasal	320.90 ± 27.12	333.53 ± 18.57	0.017	-12-62	-22.97	-2.27	0.54
Inferior	314.53 ± 24.42	330.20 ± 17.55	0.001	-15.67	-25.14	-6.20	0.73

A similar pattern was observed for macular outer thickness (MOT), where POAG patients showed significantly thinner measurements in the temporal (265.37 ± 17.78 µm vs. 277.67 ± 15.79 µm, p = 0.001, Cohen's d=0.74), superior (280.32 ± 19.60 µm vs. 290.34 ± 14.70 µm, p=0.011, Cohen's d=0.61), nasal (294.73 ± 23.32 µm vs. 307.27 ± 15.83 µm, p=0.004, Cohen's d=0.67), and inferior quadrants (265.61 ± 19.57 µm vs. 279.00 ± 13.54 µm, p=0.001, Cohen's d=0.84) (Table 3).

Table 3: Macular Outer Thickness (MOT) Across All Quadrants

Variables	Group 1, POAG (n=40)	Group 2, Controls (n=40)	p-value	Mean Difference	95%CI Lower Limit	95%CI Upper Limit	Effect Size Cohen's d
	Mean (µm) ± SD (µm)						
Temporal	265.03 ±17.87	277.63 ± 15.99	0.001	-12.60	-20.15	-5.04	0.74
Superior	279.75 ± 19.50	290.43 ± 14.87	0.007	-10.67	-18.39	-2.95	0.61
Nasal	294.18 ± 22.32	307.33 ± 16.02	0.003	-13.15	-21.80	-4.50	0.67
Inferior	264.98 ± 19.39	279.10 ± 13.70	<0.0001	-14.12	-21.60	-6.65	0.84

Macular central thickness (MCT) was also found to be lower in the POAG group (255.02± 20.882 µm) as compared to the control group (260.12± 18.021 µm), but these results were not statistically significant (p=0.240, Cohen's d=0.26). Macular total volume (MTV) was seen to be lower in the POAG group (8.01 ± 0.628 mm^3) as compared to the healthy group (8.39 ± 0.391 mm^3, p=0.001, Cohen's d=0.76) (Table 4).

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Table 4: Comparison of Macular Central Thickness (MCT) and Macular Total Volume Between Groups

Group 1, POAG (n=40)	Group 2, Controls (n=40)	p-value	Mean Difference	95%CI Lower Limit	95%CI Upper Limit	Effect Size Cohen's d
Mean (mm3) ± SD (mm^3)						
Macular Central Thickness						
255.02 ± 20.88	260.12 ± 18.02	0.240	-5.09	-13.67	3.47	0.26
Macular Total Volume						
7.99 ± 0.62	8.39 ± 0.39	0.001	-0.39	-0.63	-0.16	0.76

These findings highlight the substantial structural alterations in macular parameters associated with glaucoma, reinforcing their diagnostic significance in differentiating glaucomatous eyes from healthy eyes. Such reductions in macular thickness and volume underline the importance of these metrics as potential biomarkers for the identification of early glaucomatous damage and monitoring of POAG.

DISCUSSION

POAG leads to a gradual loss of retinal ganglion cells and their axons, which causes optic neuropathy and typical problems with a person's field of vision [1, 12]. Glaucoma leads to vision problems mainly because many retinal ganglion cell (RGC) axons and somas atrophy, stopping visual information from reaching the brain. It is believed that injury to the retinal ganglion cells and their axons happens in the optic nerve head. Because the macula has a high number of RGCs, it is now seen as a key area for checking changes in glaucoma. Even though RGCs cannot be counted directly in the living eye, retinal thickness measurements can be taken using different methods. Since retinal thickness decreases as RGCs and retinal nerve fibers are lost, measuring thickness can show the same damage. A person may have structural damage in the RNFL and optic nerve head before any obvious sight loss [5, 12]. The researchers in this study noted a strong link between thinner macular thickness and people who are Glaucoma suspects [13]. The study backs up the results by revealing a reduction in macular thickness in POAG patients, which suggests a reduction of RGCs in the macular area. Antwi-Boasiako *et al.*, showed in their research that changes in the density of RGCs in the macula observed with OCT were linked to difficulties with vision in non-human primates [14]. Similarly, Mohammadzadeh *et al.*, argued that OCT thickness of the macula is closely linked to different visual field results, so macular OCT scans should play a role in diagnosis and treatment planning for glaucoma [15]. Yadav *et al.*, performed studies that show a strong connection between thinning of the macula and the retinal nerve layer in eyes experiencing glaucomatous damage [16]. Mehta *et al.*, agreed with the study results and reported that joining GCIPL and RNFL parameters helps improve both the sensitivity and specificity for spotting the early stages of glaucoma [17]. In the study by Pedro *et al.*, using macular thickness instead of peripapillary RNFL in glaucoma screening and detecting progression offered more benefits to patients who had trouble with visual field studies [18]. We observed, as other noted, that POAG patients showed lower macular thickness inside and outside the region compared to those in the control group.

The thickness of the inner macula in POAG patients is 315.90 µm, compared to 328.84 µm in people with no disease. In the same way, POAG patients had an outer macular thickness of 275.98 µm, compared to 288.62 µm in healthy people. This pattern is strongly supported by statistics and matches what the published literature has found which confirms that macular factors are beneficial for detecting glaucoma. Doctors may use the volume of the macula as a possible marker to catch glaucoma early. The study of Nowroozzadeh *et al.*, pointed out that macular sublayer volume relates strongly to glaucoma, making it a worthy biomarker [19]. Mohammadzadeh *et al.*, proved that optical coherence tomography (OCT) volume scans can help separate patients with perimetric glaucoma from healthy individuals [20]. People with POAG showed a significantly lower mean macular volume (7.99 ± 0.62 mm^3) than healthy individuals (8.39 ± 0.39 mm^3) which again highlights its usefulness in diagnosis. It follows on from the previous studies and brings new findings, confirming a meaningful relationship between glaucomatous damage and the thickness and volume of the macula. It can assist in watching glaucoma as it progresses in both the early and more advanced phases. Research with more people and over time is required to check our conclusions and make sure the macular changes are good diagnostic and prognostic tools. The main problems making it difficult to notice developments in the macula are that there is no defined external standard and a lot of variation between repeat tests in patients. Moreover, examining the right-angle view change in the macula shown by SD-OCT and changes in visual evoked potentials and visual field tests might give a better understanding of glaucoma-related diagnosis and progression.

CONCLUSIONS

This study underlines the diagnostic value of SD-OCT in assessing macular thickness variations in patients with POAG. Our findings reveal that glaucomatous eyes have much lower macular thickness than healthy controls, with different patterns of regional thinning indicating retinal ganglion cell susceptibility. These results affirm that SD-OCT provides reliable, non-invasive, and reproducible

DOI: https://doi.org/10.54393/pjhs.v6i5.3035

measurements that can detect early glaucomatous changes, monitor progression, and potentially guide therapeutic interventions.

Authors Contribution

Conceptualization: TT

Methodology: TT, FA, AA, FK

Formal analysis: TT

Writing review and editing: MA, US

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

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