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To evaluate macular thickness and peripapillary retinal nerve fibre layer (pRNFL) thickness in primary open angle glaucoma (POAG) patients using optical coherence tomography (OCT) in semi-urban population of eastern U.P

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ABSTRACT

Aim: To evaluate macular thickness and peripapillary retinal nerve fibre (pRNFL) layer thickness in primary open angle glaucoma (POAG) patients using optical coherence tomography (OCT) in semi-urban population of eastern U.P.

Materials and Methods: Cross-sectional observational study carried out on 72eyes of 42 POAG patients and 72 eyes of 36 normal individuals above 40 years from January 2023 – August 2023 in eye OPD of Hind Institute of Medical Sciences, Barabanki. Best corrected visual acuity, anterior segment examination, Gonioscopy, tonometry, Central corneal thickness, perimetry, fundoscopy, peripapillary RNFL and macular thickness using OCT was done in all patients.

Result: POAG patients had significantly lower mean pRNFL quadrant measurements in superior, inferior and temporal quadrants when compared with controls. 83.68 ± 13.55 vs.140.01 ± 4.53; p=0.001 for superior quadrant; 76.33 ± 12.96 vs. 141.99 ± 4.51; p=0.001 for inferior quadrant; 52.31 ± 8.67 vs. 74.36 ± 3.56; p=0.001 for temporal quadrant. Mean pRNFL thickness in the nasal quadrant was not found significant in our study (55.53±7.08 vs. 80.85±5.24; p=0.295). Significant differences in thickness in foveal, inferior outer, temporal inner and nasal inner sector between POAG and control patients (p<0.05) were found.

Conclusion: Superior, inferior and temporal pRNFL quadrants thickness and foveal, inferior outer, temporal inner and nasal inner macular thickness were found to be the best parameters to diagnose POAG at early stage.

1. Introduction

Glaucoma is a chronic optic neuropathy in which slow and progressive loss of retinal ganglion cells, its axons and retinal nerve fibre layer occurs resulting in morphological changes of optic disc and defect in visual field. It is the leading cause of irreversible blindness worldwide.[1,2] Predictions are that glaucoma will affect almost 80 million people by 2020 and 111.8 million people by 2040, affecting more people residing in Asia and Africa.[3,4] The two main types of glaucoma are open angle and closed angle glaucoma. The primary open angle glaucoma (POAG) is the commonest type of glaucoma in Caucasians and Africans and constitutes about half of the primary glaucomas seen in Asians. POAG has characteristically an adult onset, rarely seen earlier than 40 years of age. It is usually bilateral, but frequently asymmetric and a cup-disc ratio

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(CDR) asymmetry of 0.2 or more is found.[5] It presents as cupping of optic disc, thinning of neuroretinal rim and by abnormalities in visual field.[6] POAG patients are generally asymptomatic or may have non-specific complaints such as headache, frequent change in presbyopic correction, noticing a 'blind spot' or scotoma and difficulty in dark adaptation. In Glaucoma retinal ganglion cells and their axons are mainly damaged. About 30 to 50% of retinal ganglion cells are located in the macular area, where these cells are arranged parallel below the nerve fibre layer (NFL) and correspond to 30 to 35% of the macular thickness (MT).[7,8] The NFL consists of axons from ganglion cells, glia cells and astrocytes. This layer becomes thicker as it approaches the optic disc, being the largest layer of the peripapillary retina.[7] Thinning of the RNFL is reported to occur even in the earliest stages of glaucoma and is thus used as a sensitive indicator of glaucomatous damage.[9–11] Macular thickness is also decreased in glaucomatous eyes.[9–13]

The structural damage with loss of retinal ganglion cells and their axons precedes functional damage, manifested by typical VF alterations.[14,15] Structural loss may occur over 5 years before the onset of functional damage, and it is thought that a 30 to 50% loss of RNFL is necessary for alterations in the VF to be detected.[8]

2. Materials and Methods

This study is a cross-sectional observational study done in eye OPD of HIMS, Barabanki over a period of 8 months from January 2023 – August 2023.

Inclusion criteria included all the diagnosed POAG patients (new and those on anti-glaucoma drugs), age more than 40 years, POAG patients having associated cataractous lens but not hampering fundal view and pseudophakic POAG patients.

Exclusion criteria included patients having narrow or closed anterior chamber angle, secondary glaucoma, diabetic retinopathy, macular degeneration, macular edema, retinal detachment or any other form of maculopathies and patients not willing to give consent.

Informed and written consent was taken from all the participants after explaining the details of the study and the procedure. Demographic data and detailed history was recorded followed by complete ocular examination and investigations which included best corrected visual acuity, anterior segment examination by slit lamp, 2 mirror Gonioscopy, Applanation tonometry, Central corneal thickness, perimetry by HFA, fundoscopy using 90D lens, peripapillary RNFL and macular thickness by using SD-OCT was done in all patients.

Peripapillary RNFL thickness was obtained in cube mode, which provided thickness measurements for all four quadrants (superior, inferior, nasal and temporal) and 12 clock hours. Macular cube mode was used to measure macular thickness. The macular thickness map was divided into nine sections (superior outer, inferior outer, nasal outer, temporal outer, superior inner, inferior inner, nasal inner, temporal inner and fovea) and the macular thickness map consists of three concentric circles: central circle, inner and outer ring, and each ring subdivided into four quadrants resulting in nine sectors (superior outer, inferior outer, nasal outer, temporal outer, superior inner, inferior inner, nasal inner, temporal inner and fovea).

Images with signal strength of 5 or more were included in analysis. Statistical analyses were performed using Microsoft Excel 2007 and IBM SPSS software (version 21.0 - SPSS Inc., Chicago, USA). P value < 0.05 was considered to be significant.

3. Result

A total of 144 eyes of 78 patients were included in the study, out of which 72 eyes of 42 patients had POAG and 72 eyes of 36 patients were normal subjects.

They were analyzed for the following parameters:

3.1. Gender distribution

Out of 72 primary open angle glaucoma eyes, 43 (59.7%) eyes were of males and 29 (40.3%) eyes were of females and of the 72 eyes of normal subjects, 40 (55.6%) eyes were of males and 32 (44.4%) eyes were of females. There was no significant difference between the two groups ($p > 0.05$).

3.2. Age distribution

In POAG group, 15.28% eyes were in the age group of 40 - <50 years, 61.11% eyes were in age group of 50 - < 60 years and 23.61% of eyes were in age group of 60 to < 70 years. In normal group, 27.78% eyes were in age group of 40 - < 50 years, 52.77% eyes in 50 - < 60 years and 19.45% eyes were in the age group of 60 - < 70 years of age. Mean age of POAG eyes were 56.06 ±5.45 years while the mean age of normal eyes were 54.17 ± 5.66 years. There was no significant difference in age between two groups ($p > 0.05$).

3.3. Best corrected visual acuity

The mean value of Log MAR BCVA in POAG eyes were 0.364 ± 0.329 and in normal eyes were 0.115 ± 0.133. The differences in BCVA between the two groups were found to be significant with p value of 0.001.

3.4. Intraocular pressure (IOP)

The mean IOP of POAG eyes was 22.90 ± 5.595 mmHg and the mean IOP of normal eyes was 15.58 ± 2.396 mmHg. It was found to be statistically significant with $p < 0.001$. Out of 72 POAG eyes, 9.72% (n = 7) of eyes had IOP between 10 to <15 mm Hg, 19.45% (n = 14) eyes had IOP between 15 to <20 mm Hg, 34.72% (n = 25) eyes had IOP between

20 to <25 mmHg, 25% (n = 18) eyes had IOP in the range of 25 to <30 mmHg and 11.11% (n = 8) eyes had IOP more than or equal to 30 mmHg. In the normal group, out of 72 eyes 43.06% (n = 31) had IOP between 10 to <15 mmHg, 50% (n = 36) eyes had IOP between 15 to <20 mmHg and 6.94% (n = 5) had IOP more than or equal to 20 mmHg.

3.5. Vertical cup to disc (C:D) ratio

The mean of vertical C:D ratio of POAG eyes was 0.703 ± 0.103 and the mean of vertical C:D ratio of normal eyes was 0.439 ± 0.081. It was found to be statistically significant with p <0.001.

3.6. Macular parameters thickness

The macular thickness were analysed in 9 sectors: fovea, superior outer (SO), inferior outer (IO), nasal outer (NO), temporal outer (TO), superior inner (SI), inferior inner (II), nasal inner (NI) and temporal inner (TI).

The mean foveal thickness in POAG eyes was 203.88 ± 12.46 μm while in control eyes was 219.03 ± 9.76 μm (p = 0.049).

The mean thickness of superior outer quadrant (SO) in POAG eyes was 225.92 ± 12.67 μm while in normal eyes was 234.25 ± 11.94 μm (p=0.854).

The mean thickness of inferior outer quadrant (IO) in POAG eyes was 211.03 ± 13.40 μm while in normal eyes was 210.97 ± 9.22 μm (p=0.008). The mean thickness of nasal outer quadrant (NO) in POAG eyes was 235.86 ± 11.86 μm while in normal eyes was 241.37 ± 11.21 μm (p=0.95).

The mean thickness of Temporal outer quadrant (TO) in POAG eyes was 201.68 ± 21.50 μm while in normal eyes was 210.78 ± 9.53 μm (p=0.17).

The mean thickness of superior inner quadrant (SI) in POAG eyes was 249.54 ± 14.86 μm while in normal eyes was 253.51 ± 11.52 μm (p=0.669).

The mean thickness of inferior inner quadrant (II) in POAG eyes was 249.22 ± 12.41 μm while in normal eyes was 259.17 ± 10.49 μm (p=0.567).

The mean thickness of nasal inner quadrant (NI) in POAG eyes was 251.22 ± 21.24 μm while in normal eyes was 267.58 ± 10.42 μm (p=0.001).

The mean thickness of temporal inner quadrant (TI) in POAG eyes was 237.99 ± 15.24 μm while in normal eyes was 250.74 ± 10.71 μm (p=0.048).

3.7. Peripapillary retinal nerve fibre layer parameters

The RNFL thickness was measured in four quadrants: superior, inferior, nasal and temporal quadrants. The mean thickness of superior quadrant in POAG eyes was 83.68 + 13.558 μm and in normal eyes was 140.01 + 4.539 μm (p = 0.001). The mean thickness of inferior quadrant in POAG eyes was 76.33 ± 12.96 μm and in normal eyes was 141.99 ± 4.514 μm (p=0.001). The mean thickness of nasal quadrant in POAG eyes was 55.53 + 7.081 μm and in normal eyes was 80.85 ± 5.245 μm (p=0.295). The mean thickness of temporal quadrant in POAG eyes was 52.31 ± 8.67 μm and in normal eyes was 74.36 ± 3.562 μm (p =0.001).

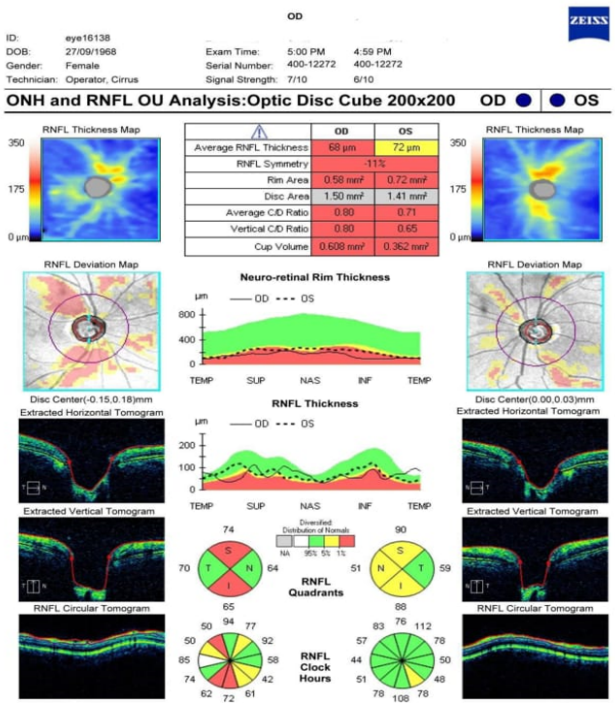

Figure 1: OCT image of peripapillary Retinal Nerve Fibre Layer in POAG patient

4. Discussion

Several studies have reported differences in RNFL thickness between normal and glaucomatous groups.[8,16] Greenfield DS et al. also studied macular thickness changes in glaucomatous optic neuropathy using optical coherence tomography and found that macular changes and visual field changes were well correlated and may be an indicator of retinal ganglion cell loss.[7] Wollstein G did Optical coherence tomography (OCT) macular and peripapillary retinal nerve fiber layer measurements and studied the correlation between macular retinal and peripapillary NFL. It was found in study that both layer thickness can help in detecting glaucomatous damage but the peripapillary nerve fibre layer thickness was more sensitive and specific for detecting visual field damage.[17] Our present study was a comparative, cross-sectional study done to determine the macular thickness and peripapillary retinal nerve fibre layer thickness in POAG patients and to find out the difference in thickness between macular and RNFL parameters in POAG eyes from those of normal eyes using SD-OCT. For this, all the 9 sectors of macular parameters (SO, IO, NO, TO,

Table 1: Mean measurements of different parameters of macular thickness in micron as measured by OCT in POAG and normal eyes

Macular Parameters	POAG (n = 72)			Normal (n = 72)			Significance
Thickness (in μm)	Mean	SD	SEM	Mean	SD	SEM	(p)
Foveal thickness	203.88	12.467	1.469	219.03	9.768	1.151	0.049
Superior Outer	225.92	12.673	1.494	234.25	11.941	1.407	0.854
Inferior Outer	211.03	13.400	1.579	210.97	9.228	1.088	0.008
Nasal Outer	235.86	11.860	1.398	241.38	11.212	1.321	0.950
Temporal Outer	201.68	21.502	2.534	210.78	9.530	1.123	0.170
Superior Inner	249.54	14.861	1.751	253.51	11.526	1.358	0.669
Inferior Inner	249.22	12.412	1.463	259.17	10.496	1.237	0.567
Nasal Inner	251.22	21.243	2.504	267.58	10.423	1.228	0.001
Temporal Inner	237.99	15.246	1.797	250.74	10.711	1.262	0.048

Table 2: Mean measurements of different parameters of pRNFL thickness as measured by OCT

RNFL thickness	POAG			Normal			Significance (p)
parameters (in μm)	Mean	SD	SEM	Mean	SD	SEM	
Superior	83.68	13.558	1.598	140.01	4.539	0.535	0.001
Inferior	76.33	12.966	1.528	141.99	4.514	0.532	0.001
Nasal	55.53	7.081	0.834	80.85	5.245	0.618	0.295
Temporal	52.31	8.670	1.022	74.36	3.562	0.420	0.001

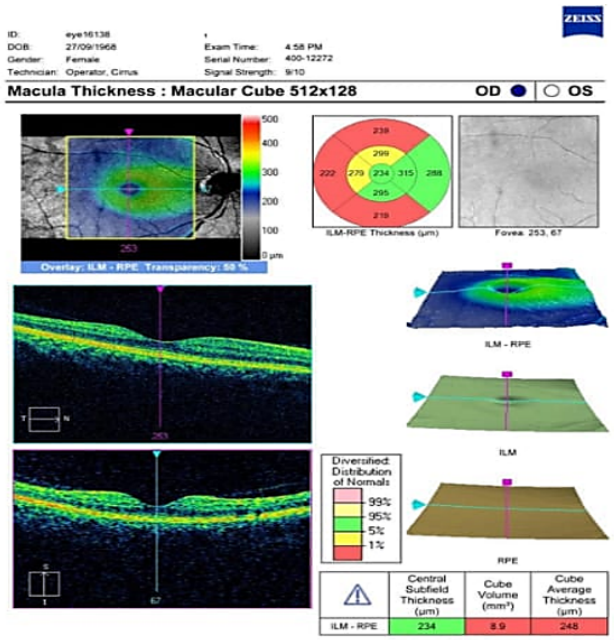

Figure 2: OCT image of Macular scan in POAG patient

SI, II, NI, TI and fovea) and RNFL parameters (Superior, inferior, nasal, temporal) of 72 eyes of 42 POAG patients were compared with those of 72 eyes of 36 normal people. In this study, out of 72 POAG eyes 43 eyes (59.7%) were of males and 29 eyes (40.3%) were of females. In the control group of 72 eyes 40 eyes (55.6%) were of males and 32 (44.4%) eyes were of females.

The mean age of POAG eyes in the study were 56.06 ± 5.454 years and of normal eyes were 54.17 ± 5.664 years. There was no significant difference in gender and age between the two groups (p = 0.332, p = 0.363 respectively) in our study. There are some studies that show men being more frequently affected by POAG as compared to females whereas others show no statistical difference between men and women.[18–20]

Comparison between patients and controls regarding the best corrected visual acuity in Log MAR value showed that POAG patients had significantly lower BCVA (0.364 ± 0.32) than the control individuals (0.115 ± 0.13) and was found to be significant (p=0.001). This finding was similar to the study of Chan et al.[21] who studied visual acuity deterioration on patients with glaucoma and concluded significant worsening of visual acuity in patients with POAG. In our study of RNFL parameters, RNFL thickness was greatest in the superior and inferior quadrants in normal group which demonstrated the so called "double hump" pattern.[22] These results were in agreement with those of the histological study done by Varma and colleagues.[23] In our study, it was shown that patients with POAG had significantly lower mean RNFL quadrant measurements in superior, inferior and temporal quadrants when compared with controls in microns (83.68 ± 13.55 vs.140.01 ± 4.53; p=0.001 for superior quadrant; 76.33 ± 12.96 vs. 141.99 ± 4.51; p=0.001 for inferior quadrant; 52.31 ± 8.67 vs. 74.36 ± 3.56; p=0.001 for temporal quadrant). The decrease in mean RNFL thickness in the nasal quadrant was not found significant in our study (55.53±7.08 vs. 80.85±5.24; p=0.295). Our findings were in accordance with the study of Nakatani and colleagues[24] who found significant differences between early glaucoma and normal participants in the superior and inferior quadrants in RNFL scans. Elbendary and Mohamed Helal[25] who evaluated

the role of SD-OCT in different stages of glaucoma also found similar results. Kanamori et al. showed in their study that inferior RNFL was the best parameter for differentiation. In a study by Saricaoglu et al, which compared Ocular hypertension (OHT) and POAG patients with normal population reported that in POAG patients there was statistically significant thinning of RNFL in all quadrants except temporal quadrant.[26]

Our findings were not consistent with the findings of Nakatani and colleagues, who reported considerable differences in all macular thickness parameters except fovea between the normal and glaucoma group. Guedes and colleagues[22] reported significant differences between normal and advanced glaucomatous groups using the standard macular thickness scan centered at the fovea in the inner ring, outer ring and mean macular thickness. The small sample size of our study may be responsible for the difference in macular scan findings in respect to other studies.

5. Conclusion

Most of the patient have good distance vision and do not notice a decline of peripheral vision. So unaware of their clinical problem, affected individuals do not seek medical advice until vision is severely decreased or the disease is detected accidentally. Therefore, it is very important that glaucoma screening be conducted regularly to help in intervening at the earliest. For this purpose OCT measurements of RNFL and macular thickness may be useful for the detection of early glaucomatous damage and may provide clinically relevant information for monitoring and follow-up of glaucoma patients. With this objective our present study was designed to evaluate the macular thickness and peripapillary RNFL thickness in POAG patients and to compare those values with the normal population to figure out if there was any significant difference between the two groups. In our study we found that certain parameters of RNFL and Macula were indeed significant. Thus, this study may be useful to clinicians in surveillance or early diagnosis of POAG. This may also be helpful in follow up of patients.

6. Limitation of the Study

Small sample size of this study is one of the limitation other being inclusion of all patients of POAG without dividing them according to their severity.

7. Source of Funding

None.

8. Conflict of Interest

None.

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