Original Research Article

Retinal nerve fibre layer analysis in primary open angle glaucoma

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Abstract

Background: POAG occurs in elderly, rarely seen earlier than 40 years of age and tends to run in families. Glaucoma is a neurodegenerative disease characterized by the slow, progressive degeneration of retinal ganglion cells.
Aim: To study the changes, in retinal nerve fibre layer thickness in primary open angle glaucoma (POAG).
Materials and methods: The present cross sectional study was carried out at a tertiary care hospital in North India. 100 patients of primary open angle glaucoma were matched with 100 controls and evaluated with the aim to assess their RNFL thickness and compare with each other.
Results: The data distribution analysis of retinal nerve fibre layer thickness in different optic nerve head quadrants in POAG group in relation to overall severity of glaucoma shows that in superior quadrant maximum number of patients in preperimetric group 6 (50%) cases, in mild 9 (45%) cases and in moderate group 25 (44.6%) were in the range 100±10μm. But in severe glaucoma cases majority 7 (58.3%) cases had the RNFL thickness in the range of 60±10 μm. The temporal quadrant RNFL thickness was least in all grades of severity of glaucoma i.e. preperimetric 6 (50%), in mild cases 9 (45%), in moderate 25 (44.6%) cases and in severe 8 (66.7%) cases.
Conclusion: Overall RNFL thickness variation, regardless of severity of glaucoma, follow the normal pattern of thickness being thicker in superior and inferior quadrant compared to nasal and temporal quadrant. It was interesting to note that the RNFL thickness in all the quadrants of optic nerve head area continues to become thinner as the severity of glaucoma increases.

Key words

Glaucoma, POAG, RNFL thickness.

Introduction

Glaucoma is a major public health problem, causing visual impairment which hampers day to day work [1].

It is the world's second leading cause of irreversible blindness [2]. Recent population-based studies from India have reported the prevalence of glaucoma blindness in those aged 40 years and older to range between 1.5% and 20% [3, 4].

POAG occurs in elderly, rarely seen earlier than 40 years of age and tends to run in families[i]. Glaucoma is a neurodegenerative disease characterized by the slow, progressive degeneration of retinal ganglion cells [5]. With glaucoma, the width of the neuroretinal rim decreases with concomitant enlargement of the cup. Glaucomatous optic neuropathy causes progressive death of retinal ganglion cells and their axons. These structural changes precede VF defects as measured by standard automated perimetry. The loss of retinal ganglion cells is considered as an important step in pathogenesis in cascade of events leading to retinal nerve fibre (RNFL) loss and changes of optic nerve head [6]. For visual field defects to be evident on white on white perimetry, it requires at least 30 -40% of neuronal cell loss to occur which is irreversible. The problem is confounded by the fact the patient is also not aware of the problem [7].

Optical Coherence Tomography (OCT) can give high resolution accurate cross section imaging of optic nerve head and macula along with the retinal nerve fibre layer analysis [8].

Materials and methods

The present cross sectional study was carried out at a tertiary care hospital in North India. 100 patients of primary open angle glaucoma were matched with 100 controls (n=200) and evaluated with the aim to assess their RNFL thickness and compare with each other. For the purpose a prospective study was planned as per the following design and methodology and all work was conducted in accordance with the declaration of Helsinki. The case group included individuals (age > 40 years) in the study group as a case of POAG only if he / she met with at least two of the following three criteria that is elevated intraocular pressure (IOP) greater than 21 mm Hg without treatment on at least two separate visit**,** Vertical asymmetry of CDR > 0.2 between two eyes and high CDR > 0.6. The control Group consisted of individuals (age >40 years) having I.O.P within normal range (11-20 mm Hg) and no glaucoma. Patients having advanced lens opacities, Prior ocular surgeries, H/O Laser treatments, Refraction–Spherical >5.0 D**,** Cylinder >3.0D, Age related macular degeneration (ARMD), Diabetes Mellitus, Hypertension were excluded from the study.

All the subjects falling in sampling frame were invited to participate in the study after fully informed consent was obtained. All cases included in the study were subjected to the similar evaluation protocol on a preset proforma. Demographic and anthropometric details were noted and a detailed personal and medical history including refractive error and diminution of vision was obtained. All the subjects underwent preliminary general and systemic examination. Clinical examination included assessment of Visual acuity by Snellen's chart, Evaluation of refractive status by Retinoscopy, IOP measurement by applanation tonometry and Direct Ophthalmoscopy, Slit Lamp Biomicroscopy was done using binoocular slit-lamp microscope and +90D lens for detailed fundus evaluation, Gonioscopy using Ziess four-mirror gonioprism. Visual field charting was done by Humphrey Field Analyser (HFA).Based on visual field analysis patients were then graded into three categories using Hodapp's classification (based on mean defect value). The grading being mild if the mean defect value was <-6 dB, moderate between -6 to -12 dB and severe if above -12dB respectively.

All included subjects were scanned with the Cirrus SD-OCT (software version 4.0) Carl-Zeiss Meditec Inc., Dublin, CA) by a single operator (ES). Scan protocol of Cirrus HD-OCT called 'optic disc cube 200 x 200' which consists of 1024 (depth) × 200 (vertical) × 200 (horizontal) data points is used for measurement of RNFL thickness. It was excluded that an image with a minimum signal strength 7/10 and below. One of the 3 scans, obtained the same day, with maximum signal strength was included. For this study, we analyzed the global average RNFL thickness, average RNFL thickness in the superior, inferior, nasal and temporal quadrants and average RNFL thickness in 12 clock hours in the 2 groups of subjects.

General Investigation: for excluding the confounding factors included Blood pressure evaluation (Normal being - Systolic 90-119 mmHg and Diastolic 60- 79 mmHg). A person is considered having hypertension when systolic blood pressure is >140 mmHg and/or diastolic blood pressure >90 mmHg[9]. Blood sugar was evaluated using the International Diabetes Federation (IDF) definitions. Fasting blood glucose >100 mg/dL was considered as raised, (IDF, 2006) [10].

Statistical analysis was done using Statistical Package for Social Sciences, version 20.0. Chi-square test was used for comparison of categorical data. Confidence level of the study was kept at 95%, hence a 'p' value less than 0.05 indicated a statistically significant association.

Results

In the present study we aimed to study the changes in retinal nerve fibre layer thickness in primary open angle glaucoma in relation to different grades of its severity and correlate RNFL thickness with visual field indices. We evaluated 100 patients of POAG and equal number of controls. Among cases there were 42 males, and 58 females, whereas among controls there were 44 males and 56 females. Majority of controls as well as patients were in the age group of 51-60 years (38 and 43 respectively). The age categories and Gender wise variation in the patients and control groups was not statistically significant. The Intraocular pressure variation among POAG cases, ranged from <20 to > 50mm Hg with overall mean IOP 31.52 ± 9.2 mmHg. In about 32 (32%) cases the ocular pressure was between 40 - 50 mmHg which was the maximum for the age group. Optic disc evaluation of 100 patients on Disc Damage likelihood Scale (DDLS) grading was done (**Table - 1**). DDLS is based on the radial width of the neuroretinal rim measured at its thinnest point. Rim/disc ratio, is the radial width of the rim compared to the diameter of the disc in the same axis. When there is no rim remaining, the rim/disc ratio is 0. There were only 2 patients (2%) with large disc DDLS grade 1. Majority cases (32%) were having DDLS grade 5 optic disc of which maximum cases had average size (1.5-2.0 mm) disc. The data distribution analysis of retinal nerve fibre layer thickness in different optic nerve head quadrants in POAG group (**Table - 2**) in relation to overall severity of glaucoma shows that in superior quadrant maximum number of patients in preperimetric group 6 (50%) cases, in mild 9 (45%) cases and in moderate group 25 (44.6%) were in the range 100± 10μm. But in severe glaucoma cases majority 7 (58.3%) cases had the RNFL thickness in the range of 60±10μm.

The Inferior quadrant optic nerve head RNFL thickness was in range of 100±10μm in maximum number of patients in preperimetric group, 7 (58.3%) while in mild glaucoma group 7 (35%) cases and in moderate glaucoma 27 (48.2%) cases the thickness was in the range 80±10 μm. In severe glaucoma group in majority 5 (41.7%) cases the RNFL thickness was further reduced in the range 60±10 μm. In Nasal optic nerve head quadrant maximum number of patients of preperimetric group, 5 (41.7%) cases had RNFL thickness in the range 80±10 μm.

However in mild glaucoma 8 (40%) cases, moderate glaucoma 25 (44.6%) cases and in severe glaucoma 6 (50%) cases had RNFL thickness in the range 60±10 µm. This shows that the RNFL thickness is worst affected in all optic nerve head quadrant.

Table – 1: Optic disc evaluation in POAG group (N=100). Disc damage likelihood scale (DDLS) grading.

OPTIC DISC (DDLS GRADE)	**SIZE OF DISC (mm)**			
	Small (<1.5)	**Average (1.5 – 2.0)**	**Large disc (>2.0)**	**Total**
0a	0	0	0	0 (0%)
0b	0	0	0	0 (0%)
1	0	0	2	2 (2%)
2	0	10	5	15 (15%)
3	0	12	3	15 (15%)
4	0	18	6	24 (24%)
5	1	26	5	32 (32%)
6	1	8	2	11 (11%)
7	0	1	0	1 (1%)

Table – 2: Data distribution RNFL thickness by OCT in POAG group (n=100).

ONH QUADRANTS	**Severity grade of POAG**	**Average RNFL thickness range (µm)**			
		120±10	**100±10**	**80±10**	**60±10**
SUPERIOR	**Preperimetric (n=12)**	5 (41.7%)	6 (50%)	1 (8.3%)	0 (0%)
	Mild (n=20)	2 (10%)	9 (45%)	6 (30%)	3 (15%)
	Moderate (n=56)	3 (5.4%)	25 (44.6%)	18 (32.1)	10 (17.8%)
	Severe (n=12)	0 (0%)	2 (16.7%)	3 (25%)	7 (58.3)
INFERIOR	**Preperimetric (n=12)**	4 (33.3%)	7 (58.3%)	1 (8.3%)	0 (0%)
	Mild (n=20)	2 (10%)	6 (30%)	7 (35%)	5 (25%)
	Moderate (n=56)	5 (8.9%)	12 (21.4%)	27 (48.2%)	12 (21.4%)
	Severe (n=12)	0 (0%)	3 (25%)	4 (33.3%)	5 (41.7%)
NASAL	**Preperimetric (n=12)**	0 (0%)	3 (25%)	5 (41.7%)	4 (33.3%)
	Mild (n=20)	0 (0%)	5 (25%)	7 (35%)	8 (40%)
	Moderate (n=56)	0 (0%)	11 (19.6%)	20 (35.7%)	25 (44.6%)
	Severe (n=12)	0 (0%)	2 (16.7%)	4 (33.3%)	6 (50%)
TEMPORAL	**Preperimetric (n=12)**	0 (0%)	3 (25%)	3 (25%)	6 (50%)
	Mild (n=20)	0 (0%)	4 (20%)	7 (35%)	9 (45%)
	Moderate (n=56)	0 (0%)	12 (21.4%)	19 (33.9%)	25 (44.6%)
	Severe (n=12)	0 (0%)	1 (8.3%)	3 (25%)	8 (66.7%)

The temporal quadrant RNFL thickness was least in all grades of severity of glaucoma i.e. preperimetric 6 (50%), in mild cases 9 (45%), in moderate 25 (44.6%) cases and in severe 8 (66.7%) cases.

The above observations clearly show that the overall RNFL thickness variation, regardless of severity of glaucoma, follow the normal pattern of thickness being thicker in superior and inferior quadrant compared to nasal and temporal quadrant. It was interesting to note that the RNFL thickness in all the quadrants of optic nerve head area continues to become thinner as the severity of glaucoma increases.

Further a comparative evaluation of average RNFL thickness in control and cases was done

(**Table - 3**), it reveals that the difference in the average thickness of each Retinal Nerve Fibre Layer quadrant compared to normal is highly statistically significant. The thinning of RNFL is constant feature in each quadrant of Optic Nerve Head in POAG cases.

<u>Table – 3</u>: Comparative evaluation RNFL thickness (μm).
Control v/s Case (POAG) group

ONH QUADRANT (Average)	**CONTROL (*n*=100)**	**POAG (*n*=100)**	**p value**
Superior quadrant	130.0±19.5	93.72±19.9	0.001
Nasal quadrant	82.97±18.5	90.51±17.6	0.001
Inferior quadrant	135.4±19.2	63.63±18.4	0.001
Temporal quadrant	74.23±17.8	57.66±18.9	0.037
Average	105.65±18.6	89.67±18.9	0.001

Discussion

Establishing the severity of glaucoma has largely been based on perimetric parameters [11], It has been shown that damage to the retinal nerve fiber layer (RNFL) precedes visual field loss [12]. Quigley, et al. [13] reported that up to 40% to 50% of the RNFL could be lost before visual field defects are detected by conventional perimetry. Thus, RNFL assessment has emerged as an important parameter for preperimetric diagnosis of glaucoma.

Optical coherence tomography (OCT) is a noncontact, noninvasive diagnostic technique that allows measurement of RNFL thickness by in vivo visualization of the retina and RNFL with good reproducibility [14-18]. In present study, Optic disc evaluation of 100 patients on Disc Damage likelihood Scale (DDLS) grading was done (**Table - 1**). DDLS is based on the radial width of the neuroretinal rim measured at its thinnest point. Rim/disc ratio, is the radial width of the rim compared to the diameter of the disc in the same axis. When there is no rim remaining, the rim/disc ratio is 0. There were only 2 patients (2%) with large disc DDLS grade 1. Majority cases (32%) were having DDLS grade 5 optic disc of which maximum cases had average size (1.5-2.0 mm) disc. Anuradha Chandra, et al. [19] in their study used optic disc sizes as parameter for evaluation they were in ranges from 1.5 mm to 2.5 mm with average vertical disc size 2.0307 mm (SD = 0.2311). The data distribution analysis of retinal nerve fibre layer thickness in different optic nerve head quadrants in POAG group (**Table - 3**) in relation to overall severity of glaucoma shows that in superior quadrant maximum number of patients in preperimetric group 6 (50%) cases, in mild 9 (45%) cases and in moderate group 25 (44.6%) were in the range 100± 10μm. But in severe glaucoma cases majority 7 (58.3%) cases had the RNFL thickness in the range of 60±10μm.

The Inferior quadrant optic nerve head RNFL thickness was in range of 100±10μm in maximum number of patients in preperimetric group, 7 (58.3%) while in mild glaucoma group 7 (35%) cases and in moderate glaucoma 27 (48.2%) cases the thickness was in the range 80±10 μm. In severe glaucoma group in majority 5 (41.7%) cases the RNFL thickness was further reduced in the range 60±10 μm.

Cvenkel B, et al. [20] (2011) and Ramanjit Sihota, et al. [21] also reported the differences in RNFL thickness between normal and glaucoma eyes were significant ($p < 0.001$) for all measurements. The above observations clearly show that the overall RNFL thickness variation, regardless of severity of glaucoma, follow the normal pattern of thickness being thicker in superior and inferior quadrant compared to nasal and temporal quadrant. It was interesting to note that the RNFL thickness in all the quadrants of optic nerve head area continues to become thinner as the severity of glaucoma increases.

Conclusion

Overall RNFL thickness variation, regardless of severity of glaucoma, follow the normal pattern of thickness being thicker in superior and inferior quadrant compared to nasal and temporal quadrant. It was interesting to note that the RNFL thickness in all the quadrants of optic nerve head area continues to become thinner as the severity of glaucoma increases.

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