Research Article

Retinal Nerve Fibre Layer Analysis in Non-Glaucomatous Pseudoexfoliation Syndrome Patients

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Abstract

Pseudoexfoliation Syndrome (PXS) is a disorder characterized by the progressive accumulation of fibrillary extracellular deposits in several ocular tissues. It is an independent risk factor for glaucomatous optic nerve damage. Retinal Nerve Fiber Layer (RNFL) thickness analysis using optical coherence tomography is a documented investigative tool to detect glaucoma at an early stage. The aim was to evaluate and compare RNFL thickness in PXS patients without glaucoma with their age and sex matched healthy controls and to detect the possibility of early glaucomatous damage in patients with RNFL thinning. A total of 100 patients were included, of which 50 were cases (Group A) and 50 were controls (Group B). RNFL thickness of cases and controls were compared using Zeiss Cirrus HD-OCT 500.

There were no significant differences between the two groups with respect to mean RFNL thickness in nasal ($p = 0.129$) and temporal quadrants ($p = 0.925$). Mean inferior RNFL thickness was 112.9 ± 21.72 μm in Group A and 120.6 ± 10.35 μm in Group B ($p = 0.002$). The mean thickness of retinal nerve fiber layer in superior quadrant in Group A was 101.6 ± 23.16 μm whereas in group B it was 113.5 ± 13.47 μm. ($p< 0.001$). The average RFNL thickness in Group A was 85.1 ± 13.99 μm and in Group B it was 88.9 ± 7.01 μm. ($p = 0.017$). There was statistically significant difference in RNFL thickness between cases and controls in inferior and superior quadrants and in global average thickness.

Keywords: Pseudoexfoliation syndrome; Glaucoma; Retinal nerve fiber layer

Introduction

Glaucoma is a leading cause of irreversible blindness throughout the world. Pseudoexfoliation Syndrome (PXS) is the most common identifiable cause of open-angle glaucoma worldwide.

PXS is an age-related, genetically determined, generalized disorder of the extracellular matrix characterized by production and progressive accumulation of a fibrillar material in ocular tissues, skin and other visceral organs.

Its ocular manifestations affect all of the structures of the anterior segment as well as conjunctiva and orbital tissues [1]. It is the Optic Nerve Head [ONH] and the Retinal Nerve Fibre Layer (RNFL) containing retinal ganglion cell axons that are most clearly associated with glaucomatous vision loss especially the circumpapillary RNFL.

Pseudoexfoliative Glaucoma [PXG] tends to progress slowly and patients are often asymptomatic until the disease reaches an advanced stage. PXG represents a relatively severe and progressive type of glaucoma, with a generally poor prognosis due to high intraocular pressure levels, great pressure differences between the two eyes and fluctuations in the diurnal pressure curve.

Optic neuropathy due to glaucoma is largely irreversible, so early detection and prevention is of vital importance.

Structural damage of ONH and RNFL may precede functional loss and it is estimated that between 30-50% of retinal ganglion cells may be lost before detectable changes in visual fields are evident.

Spectral domain optical coherence tomography (SD-OCT) provides high resolution, quantitative and reproducible measurements of RNFL having high sensitivity and specificity for differentiating normal eyes from patients with early glaucoma [2]. OCT has a well known role in diagnosing pre-perimetric glaucoma. This study was done to compare mean RNFL thickness in patients having PXS with normal age matched healthy controls using SD-OCT.

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Materials and Methods

This prospective case control study was conducted in Sher-e-Kashmir Institute of Medical Sciences Medical College and Hospital, Srinagar, Jammu and Kashmir, India, in the Postgraduate Department of Ophthalmology from October 2017 to April 2019, after approval of hospital ethical committee. A written consent was obtained from the patients. A total of 100 patients were included in this study, of which 50 were cases (Group A) which included nonglucomatous PXS patients and 50 were their age and sex matched healthy controls (Group B). 88 eyes in Group A were examined, as 12 patients had unilateral pseudoexfoliation and 100 eyes in Group B were examined. The diagnosis of pseudoexfoliation (PEX) was made on the basis of following findings: PEX material on the lens capsule or near the pupil; transillumination defects near the pupil; Increased pigmentation or PEX material at the angle, or both [3]. An eye was considered normal if it had an IOP of < 21 mmHg, an optic disc with normal ophthalmoscopic appearance and normal visual field test results. All participants underwent a complete ocular examination. Biomicroscopic and fundoscopic examination with a 90 dioptre lens was performed, and IOP was measured using a Goldmann applanation tonometer. Visual field evaluation was done using the 30-2 SITA-Standard algorithm (Humphrey Visual Field Analyser). OCT was done by Cirrus HD 500 spectral domain OCT.

Inclusion Criteria:

- Presence of pseudoexfoliative material on the pupil margin or on the lens capsule on bio-microscopic evaluation
- Intra ocular pressure equal to or less than 21 mmHg
- Normal optic nerve head appearance (with C/D ratio 0.3-0.4)
- Normal visual field analysis on humphery field analyser.

Exclusion Criteria:

- Glaucomatous patients or family history of glaucoma
- Media opacity interfering with visualization and OCT image capturing
- History of any ocular diseases
- Previous ocular trauma
- Any retinal pathology
- History of diabetes mellitus.

All data were analyzed using SPSS software 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD and categorical variables were summarized as frequencies and percentages [4]. Student's independent t-test was employed for comparing continuous variables. Chi-square test or Fisher's exact test, whichever appropriate, was applied for comparing categorical variables. Fundus changes were compared using Mann Whitney U-test. A p-value of less than 0.05 was considered statistically significant.

Results

Mean age of Group A (cases) was 63.3 ± 6.98 years and of Group B (control) was 63.9 ± 6.81 years (p = 0.68), and most of the patients were in the range of 60–69 years. Both groups were gender matched with female preponderance. Mean IOP was comparable in both groups. Mean IOP in PEX group was 16.91 ± 1.76 mmHg and 16.85 ± 1.91 mmHg in control group (p=0.83) (Table 1).

Table 1: Patient Demographic Profile with Intraocular pressure (IOP)

	Cases (Group A)		Controls (Group B)	
Age in years (Mean ± SD)	63.3 ± 6.98		63.9 ± 6.18	
Gender	0.48	Males	0.46	Males
	0.52	Females	0.54	Females
IOP in mm Hg (Mean ± SD)	16.91 ± 1.759		16.85 ± 1.909	

The mean RNFL measurements at each location are shown in Table2. Mean superior RNFL thickness was 101.6 ± 23.16 µm in Group A and 113.35 ± 13.47 µm in Group B (p < 0.001). Mean inferior RNFL thickness was 112.9 ± 21.72 µm in Group A and 120.6 ± 10.35 µm in Group B (p = 0.002). Mean nasal RNFL thickness was 63.1 ± 10.9 µm in Group A and 63.4 ± 9.98 µm (P =0.129) in Group B. Mean temporal RNFL thickness was 57.3 ± 13.12 µm and 57.3 ± 9.56 µm in Group A and B, respectively (P = 0.925) . Mean average peripapillary RNFL thickness was 85.1 ± 13.99 µm in Group A and 88.9 ± 7.01 µm in Group B (p < 0.10) (Table 2 and Figure 1).

Table 2: Quadrant wise RNFL thickness

RNFL THICKNESS	CASES (GROUP A) N=88(EYES)	CONTROLS (GROUP B) N=100 (EYES)	P VALUE

SUPERIOR (µm)	101.6 ± 23.16	113.5 ± 13.47	< 0.001
INFERIOR (µm)	112.9 ± 21.72	120.6 ± 10.35	0.002
NASAL (µm)	63.1±10.9	63.4±9.98	0.129
TEMPORAL (µm)	57.5 ± 13.12	57.3 ± 9.56	0.925
GLOBAL AVERAGE (µm)	85.1 ± 13.99	88.9± 7.01	0.017

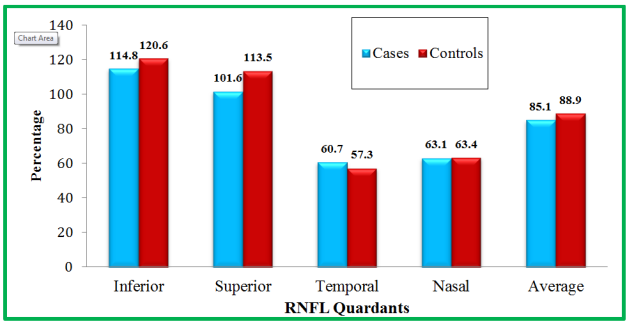

Figure 1: Quadrant wise comparison of RFNL thickness

Discussion

Secondary chronic open-angle glaucoma associated with PXS accounts for approximately 25% of all glaucoma and represents the most common identifiable cause of glaucoma overall . Optic disc evaluation by slit lamp biomicroscopy or photography is subjective and causes inter-observer variability. Gold standard test for detection of glaucomatous optic nerve damage is Visual field analysis, however, abnormality is detected only after 40% loss of retinal ganglion cell has occurred. Glaucoma is identified biologically by the death of retinal ganglion cells. As retinal ganglion cells are lost, the retinal nerve fibers are also lost, and this layer thins. Thus, RFNL defect is a main sign of early glaucomatous damage and that visual field testing, fundus image and IOP may not be sensitive to detect this early damage. Structural damage of ONH and RNFL may precede functional loss.The high diagnostic accuracy of the SD OCT allows for rapid, reproducible OCT scanning of the RNFL thickness and monitors changes in thickness for the detection of early glaucoma.

The aim of this study was to detect early RNFL damage in pseudoexfoliative patients without glaucoma by measuring RNFL thickness using SD OCT and comparing the results with age matched healthy control subjects. In our study, mean RFNL thickness in inferior quadrant showed statistically significant thinning in patients with PXS vs healthy controls (112.9 vs 120.6; p = 0.002). The present study also showed statistically significant thinning of RNFL in superior quadrant of BOTH PXS and control groups (101.6 vs 113.5; p< 0.001). The RFNL in nasal quadrant was thinner in PXS group than in controls but was not statistically significant(p =0.129) . In temporal quadrant the RNFL was thicker in PXS group but there was no statistically significant difference in thickness of RNFL among PXS and controls groups. (0.925) This study also revealed thinner mean Global average peripapillary RNFL thickness in PXS group as compared to the control group [5].

In the early stage of PXG, RNFL defect usually progresses to affect mainly local areas in the superior and/or inferior pole. However, with more progression of disease it becomes more extensive and shows diffuse and combination RNFL defects. This study revealed thinner mean Global average peripapillary RNFL thickness in cases as compared to the control group.

Analysed retinal nerve fiber layer thickness in patients with pseudoexfoliation syndrome using SD OCT. The RNFL thickness in normal subjects was normally thicker in the superior and inferior, thinner in the temporal and lowest in the nasal quadrants; however in PXS group; there were significant differences in RNFL thickness among the four quadrants except for the nasal quadrant compared to the control group. This could be explained by the fact that higher axonal density and higher proportion of large fibers occupies the superior and inferior portions of the optic nerve head compared to the temporal and nasal portion. These fibers (superior and inferior) are in addition most susceptible to early glaucomatous damage.

In the study by MM Mohamed, the early glaucomatous changes in pseudoexfoliation syndrome patients was assessed. He found statistically significant thinning of RNFL in temporal, superior and inferior quadrants.

Another study was done comparing RNFL thickness in PXS patients with normal subjects. Although they found thinner mean RFNL thickness in all quadrants but the difference was statistically significant only in the inferior quadrant. Most of the work done on measurement of RNFL thickness in PXS without glaucoma using different OCT machines revealed thinner mean global peripapillary RNFL in eyes with PXS as compared to control group with some variations in quadrantic measurements that may be attributed to variation in age, sample size, ethnicity and type of OCT machine used.

Although results of our study corresponds with the results of international studies, some variation in absolute values was found that may be attributed to variation in age, ethnicity, gender distribution, machine used and normative data. This study gives some insight into diagnosing pre-perimetric glaucoma using OCT as PXS patients with normal IOP and visual fields were tested and found to be having thin RNFL than their age matched adults.

Conclusion

The results of this study show that the eyes with PXS are associated with significant decrease in RNFL thickness and detecting this thinning in eyes of PXS patients without glaucomatous change will help in early detection of patients at risk of glaucoma. Such PXS patients without glaucoma having RNFL thinning will be considered as a high-risk group for the development of glaucoma and will be kept on regular follow up.

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