Innovations

Evaluating the Changes in Retinal Nerve Fiber Layer in Patients with Varying Degrees of Pseudoexfoliation

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Abstract
Background: *Pseudoexfoliation (PEX) syndrome is a systemic, age-related disorder primarily affecting older individuals. It is characterized by the deposition of abnormal fibrillar material known as pseudoexfoliation material (PEM), which accumulates in the anterior segment of the eye, particularly at the pupillary margin, lens surface, and zonules. In addition to ocular structures, PEM can deposit in various extraocular tissues, including the skin, lungs, heart, liver, kidneys, and meninges, making PEX a widespread systemic condition.* ***Aims & Objectives***: *The impact of varying grades of pseudoexfoliation on the thickness of the retinal nerve fibre layer (RNFL) in patients with pseudoexfoliation syndrome.* ***Methodology***: *A prospective, cross-sectional study was conducted on 96 eyes diagnosed with pseudoexfoliation (PEX) ,after grading patients with RNFL thickness of optic disc were analyzed with standard OCT protocol in all subjects .****Results***: *Total 96 patients, 62 males and 34 females. The agerange of the study participants was between 40 and 80 years ,with a mean age of 65.1± 5.4years. In our study , there was association between superior, Nasal as well as Temporal quadrant retinal layer thickness and degree of pseudiexfoliation. there was significant RNFL thinning in severe PEX compared to mild and moderate PEX. Average RNFL thickness declined progressively from mild (85.4 ± 19.3 μm) to moderate (77.1 ± 16.5 μm) and severe PEX (61.7 ± 14.2 μm), with the difference being highly statistically significant (ANOVA, $F = 29.36$, $p < 0.001$), indicating greater RNFL thinning with increasing disease severity.* ***Conclusion***: *The study's findings indicate that PXS patients have much thinner RNFL and identifying this thinning in PXS patient's eyes will aid in the early identification of glaucoma. Average RNFL thickness shows a progressive decline from mild to severe PEX, indicating that RNFL thinning significantly worsens with increasing disease severity. These PXS patients with RNFL thinning who do not have glaucoma should be monitored often since they are deemed to be at high risk for developing glaucoma.*

Keywords: *Retinal Nerve, Pseudoexfoliation, Vision, Outcome.*

Introduction: Pseudoexfoliation is afibrillar substance which is typically observed in the anterior segment, pupils, and extraocular tissues including the skin and deposited gradually in exfoliation syndrome (XFS), a systemic condition [1]. The most prevalent secondary open-angle glaucoma is exfoliative glaucoma (XFG) which arises when PEX material and pigment clog the trabecular meshwork[2].

In people with XFS, intraocular pressure (IOP) get elevated and fluctuate. Thus, this may result in XFG which progresses more quickly than primary open-angle glaucoma (POAG) [3]. The presence of PEX material has been found to be the most significant independent risk factor for the advancement of glaucoma, and patients with XFS are more likely to sustain optic nerve injury at a particular level of IOP [4,5]. The corneal endothelium, anterior lens capsule, and trabecular meshwork are examples of anterior segment structures that PEX material can influence. It has also been demonstrated that PEX material can influence posterior segment structures like the posterior ciliary arteries, vortex veins, and central retinal veins [6].

The incidence of pseudoexfoliation increases with ageand unilateral involvement is observed in approximately two-thirds of patients. At the time of diagnosis, pseudoexfoliation material can also be found on the lens surface in the contralateral eye, even in the absence of classical accumulation on conjunctival biopsy. One of the earliest signs of glaucomatous changes in PEXG is thinning of the retinal nerve fiber layer (RNFL). The RNFL is crucial for transmitting visual information from the retina to the brain and its degeneration is often an early indicator of optic nerve damage.The severity of pseudoexfoliation correlates with an increased risk of developing glaucoma, particularly pseudoexfoliation glaucoma (PEXG), which leads to optic nerve damage and progressive visual field loss. [8,9,10,11]So, present study was conducted to assess the impact of varying grades of pseudoexfoliation on the thickness of the retinal nerve fibre layer (RNFL) in patients with pseudoexfoliation syndrome.

Aims & Objectives: The impact of varying grades of pseudoexfoliation on the thickness of the retinal nerve fibre layer (RNFL) in patients with pseudoexfoliation syndrome.

Methodology:

A prospective, cross-sectional study was conducted on 96 eyes diagnosed with pseudoexfoliation (PEX) in the Department of Ophthalmology at R.L.J. Hospital and Research Centre, Kolar attached to Sri DevarajUrs Medical College. Patients of aged 50 years or older of either gender with unilateral or bilateral pseudoexfoliation were included. Patients with a history of primary or secondary glaucoma, Patients retinal diseases (e.g., diabetic retinopathy, age-related macular degeneration), Patients with ocular conditions affecting RNFL (e.g., optic neuropathies), Patients with intraocular pressure >21 mmHg. Patient with media opacities were excluded. A total of 96 eyes of patients , fulfilling the inclusion criteria will be included in this study. After obtaining a detailed history and demographic data, each patient was clinically examined by the following: Visual acuity assessment by using the Snellen chart for distant vision,Slit lamp biomicroscopy for evaluation of the anterior segment.Gonioscopy to visualize the anterior chamber angles, Posterior segment evaluation is done by indirect ophthalmos copy and +90D biomicroscopy, Assessment of intraocular pressure by Goldmann Applanation Tonometer, SD-Optical coherence tomography (OCT) is used for measuring OPTIC NERVE HEAD AND RNFL. The eyes will be classified based on the extent of PEX material deposition as follows:

1. Mild: PEX material present on part of the pupillary border.
2. Moderate: PEX material present along the entire pupillary border.
3. Severe: PEX material present on the entire pupillary border and extending onto the iris surface.

Data Entry & Analysis:

Data was collected in Microsoft Excel sheet and analysed by using SPSS software version 26. Quantitative data is described as Mean and SD and qualitative data are described as frequency and percentages. The chi square test z test for means and Anova test was used. p value less than 0.05 is considered as a statistically significant.

Results:

Total 96 patients, 62 males and 34 females. The age range of the study participants was between 40 and 80 years, with a mean age of 65.1± 5.4 years. No statistically significant differences were observed between the research groups in terms of sex and age groups.

Table1: Distribution as per Degree of Pseudoexfoliation

The degree of pseudoexfoliation	Frequency N=96	Percentage
Mild	31	32.3
Moderate	33	34.3
Severe	32	33.4

On assessing, 31(32.3%) cases had Mild PEX, 33(34.4%) cases had moderate PEX and 32(33.4%) cases had severe PEX. [Table 1]

Table2: Comparison of Superior Quadrant with the Degree of Pseudoexfoliation

Superior Qudrant	Mild PEX	Moderate PEX	Severe PEX	P-value
Mean ± SD	124.5±24.4	122.32±19.7	116.3±20.7	0.001

The mean Superior Quadrant value was 124.5±24.4, 122.32±19.7 and 116.3±20.7, respectively in Mild ,Moderate and Severe PEX. There are statistically significant differences found between Superior Quadrant with the Degree of Pseudoexfoliation.

Table3:Comparison of Inferior Quadrant with the Degree of Pseudoexfoliation

Inferior Quadrant	Mild PEX	Moderate PEX	Severe PEX	P-value
Mean ± SD	121.62±9.8	122.85±11.6	122.4± 12.9	0.0432

The mean Inferior Quadrant value was 121.62±9.8, 122.85±11.6 and 122.4± 12.9,respectively in Mild ,Moderate and Severe PEX.There are no statistically significant differences were observed between the research groups.

Table 4: Comparison of Nasal Quadrant with the Degree of Pseudoexfoliation

Nasal Quadrant	Mild PEX	Moderate PEX	Severe PEX	P-value
Mean ±SD	82.1±7.3	76.3±8.2	69.1± 11.3	0.001

The mean Nasal Quadrant value was 82.1±7.3, 76.3±8.2 and 69.1± 11.3respectively in Mild ,Moderate and Severe PEX.There are statistically significant differences between Nasal Quadrant with the Degree of Pseudoexfoliation .

Table 5: Comparison of the Temporal Quadrant with the Degree of Pseudoexfoliation

Temporal Quadrant	Mild PEX	Moderate PEX	Severe PEX	P-value
Mean ± SD	64.9 ± 4.9	65.2 ± 6.6	63.4 ± 5.7	0.326

The mean Temporal Quadrant value was 64.9 ± 4.9, 65.2 ± 6.6 and 63.4 ± 5.7respectively in Mild ,Moderate and Severe PEX.There are no statistically significant differences between Temporal Quadrant with the Degree of Pseudoexfoliation.

Table 6. Comparison of various quadrant vision and Degree of Pseudoexfoliation

Quadrant wise retinal layer thickness		Mild PEX	Moderate PEX	Severe PEX	P value
Superior	< 120	2	8	15	0.0091
	120-140	13	11	7	
	> 140	16	14	10	
Inferior	< 120	5	9	9	0.197

	120-140	15	7	9	
	> 140	11	17	14	
Nasal	< 70	4	6	14	0.0313
	70-90	10	12	10	
	> 90	17	15	8	
Temporal	< 60	3	8	13	0.0482
	60-80	8	11	7	
	> 80	20	14	12	

In the superior quadrant, the number of cases with retinal thickness <120 μm increased with PEX severity (2 in mild, 8 in moderate, 15 in severe), suggesting thinning with disease progression. Conversely, cases with thickness >140 μm were more frequent in mild PEX (16), decreasing in moderate (14) and severe cases (10). In the inferior quadrant, similar trends were observed. The count of cases with thickness <120 μm was lowest in mild PEX (5), rising in moderate (9) and severe PEX (9). The group with thickness >140 μm had the highest number in moderate PEX (17), indicating some variability in distribution compared to the superior quadrant. The nasal quadrant showed a notable increase in patients with <70 μm thickness in severe PEX (14 cases), compared to 4 in mild and 6 in moderate PEX. Those with thickness >90 μm were mostly seen in mild (17) and moderate PEX (15), dropping to 8 in severe PEX, again suggesting retinal thinning with disease progression. For the temporal quadrant, thickness <60 μm was seen in 3 cases of mild, 8 moderate, and 13 severe PEX, while >80 μm was most common in mild PEX (20), followed by moderate (14) and severe (12), continuing the overall trend of decreased retinal thickness with increasing severity of PEX. On applying chi square test, there was association between superior, Nasal as well as Temporal quadrant retinal layer thickness and degree of pseudiexfoliation. [Table 6]

GRADES OF PEX	AVERAGE RNFL THINNING
MILD	85.4 +/-19.3
MODERATE	77.1+/-16.5
SEVERE	61.7+/-14.2

Average RNFL thickness declined progressively from mild (85.4 ± 19.3 μm) to moderate (77.1 ± 16.5 μm) and severe PEX (61.7 ± 14.2 μm), with the difference being highly statistically significant (ANOVA, F = 29.36, p < 0.001), indicating greater RNFL thinning with increasing disease severity.

Discussion: Although the exact process causing open-angle glaucoma is still unknown, XFS is the most significant recognized risk factor for the condition [12]. In conditions like glaucoma, when ganglion cells are lost, the RNFL thickness diminishes. Measurement of RNFL thickness is helpful for glaucoma follow-up and early diagnosis [13,14]. By enabling early detection and treatment, a reduction in RNFL thickness before to the onset of visual field defect can stop the course of glaucoma [15].

PEX material has been linked to RNFL reduction in studies of eyes with XFS. Vergados et al. found that a group with XFS had a thinner RNFL than a control group [16]. Yu et al. found that a group with XFS had significantly less RNFL thickness than a control group. In order to detect early glaucomatous damage and start treatment before visual field loss occurs, those authors also emphasized the significance of assessing RNFL thickness using OCT in patients with XFS [17].

Although only the inferior quadrant showed a significant difference, Özmen et al. also noted a thinner RNFL in an XFS group as compared to a control group [18]. According to Puska et al., PEX material might increase the probability of ganglion cell death in XFS and XFG, regardless of IOP [19].

In patients with XFS, a decrease in RNFL thickness could indicate that exfoliating agents alone are risk factors that cause glaucomatous damage. In order to identify glaucomatous damage in eyes with XFS, RNFL assessment with OCT is crucial. Exfoliating substances have been demonstrated to have the ability to influence the posterior region, including the ciliary arteries, vortex veins, and central retinal veins, in addition to the anterior ocular segment. Furthermore, research has shown that it reduces blood flow to the eyes [20]. In their investigation of retrobulbar hemodynamics and ocular perfusion pressure, Galassi et al. found that patients with XFG had worse retrobulbar hemodynamics and lower ocular perfusion pressure than healthy people [21].

Conclusion: The study's findings indicate that PXS patients have much thinner RNFLs, and identifying this thinning in PXS patients' eyes without glaucomatous changes will aid in the early identification of glaucoma risk. These PXS patients with RNFL thinning who do not have glaucoma will be monitored often since they are deemed to be at high risk for developing glaucoma.

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