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Original Article

Retinal Nerve Fiber Layer Thickness in Pseudoexfoliation Syndrome: A Case-Control Study with Literature Integration

Dr. Kriti Tiwari[1], Dr. Aishwarya Raghuwanshi[2], Dr. Deepanshi Agrawal[3]

[1]Post graduate student, Department of Ophthalmology, Chirayu Medical College and Hospital, Bhopal, India,
[2]Assistant Professor Department of Ophthalmology Chirayu Medical College and Hospital Bhopal, India,
[3]Post graduate student, Department of Ophthalmology, Chirayu Medical College and Hospital, Bhopal, India

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Corresponding Author:

Dr. Kriti Tiwari
kritimanju@gmail.com

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ABSTRACT

Purpose: To compare peripapillary retinal nerve fiber layer (RNFL) thickness in patients with pseudoexfoliation syndrome (PXF) and age-matched healthy controls, and to integrate the findings with prior studies and meta-analysis data.
Methods: This case-control observational study included 30 eyes with clinically diagnosed Pseudoexfoliation without glaucoma and 30 age-matched healthy controls aged >40 years. Intraocular pressure (IOP) was measured using Goldmann applanation tonometry, and RNFL thickness in the superior, inferior, nasal, and temporal quadrants was assessed using spectral domain OCT. Data were analyzed using SPSS v20; $p < 0.05$ was considered statistically significant.
Results: Mean RNFL thickness was significantly lower in the Pseudoexfoliation group than in controls (76.9 µm vs 84.2 µm; $p = 0.016$). The inferior quadrant showed the most marked thinning (88.4 µm vs 100.4 µm; $p = 0.011$), while superior (82.3 µm vs 86.5 µm; $p > 0.05$), nasal (65.1 µm vs 68.7 µm; $p > 0.05$), and temporal (58.6 µm vs 61.2 µm; $p > 0.05$) quadrants were not significantly different. The findings are consistent with the meta-analysis by Yu et al. (2017) and the study by Yasmeen et al. (2016), both of which reported significant RNFL loss in Pseudoexfoliation, particularly in the inferior quadrant.
Conclusion: RNFL thinning is evident in Pseudoexfoliation patients even without elevated IOP or glaucomatous visual field defects. The inferior quadrant is the most consistently affected region. These findings support routine SD-OCT screening in Pseudoexfoliation patients for early detection of optic nerve damage.

Keywords: *Pseudoexfoliation syndrome; retinal nerve fiber layer; spectral-domain OCT; glaucoma; optic nerve damage.*

INTRODUCTION

Pseudoexfoliation syndrome is an age-related systemic microfibrillopathy characterized by deposition of abnormal fibrillar extracellular material on ocular structures such as the anterior lens capsule, ciliary body, and trabecular meshwork. It is strongly associated with secondary open angle glaucoma due to impaired aqueous outflow and progressive optic nerve damage. [7-9]. Glaucomatous injury is often preceded by structural changes in the retinal nerve fiber layer. Spectral domain optical coherence tomography (SD-OCT) provides a non-invasive, high resolution method for detecting subtle RNFL thinning, even before functional visual field defects appear. Several studies have demonstrated significant RNFL thinning in patients with PXF, including those with normal IOP and normal visual fields. [1-6, 10, 11]. Yu et al. (2017) conducted a meta-analysis of eight case-control studies (225 PXF eyes vs 208 controls) and reported a mean RNFL reduction of 6.91 µm (95% CI: −9.99 to −3.82; $p < 0.0001$), with significant thinning in all quadrants. Yasmeen et al. (2016) similarly found thinner average RNFL (77.5 ± 12.2 µm vs 84 ± 10.6 µm; $p = 0.020$) and significant inferior quadrant thinning ($p = 0.014$) in a Pakistani cohort of 35 PXF eyes. [1, 2]. The present study evaluates peripapillary RNFL thickness in Pseudoexfoliation eyes without glaucoma, compares these values with healthy age-matched controls, and discusses the results in light of these prior reports.

METHODS

Study design and participants: This was a case-control observational study conducted in the Department of Ophthalmology from April to July 2024. Sixty eyes (one eye per subject randomly to avoid inter eye correlation bias) were

enrolled. The sample size was determined based on an expected difference of approximately 6–7 µm in mean RNFL thickness between pseudoexfoliation and control groups, as reported in previous studies. Assuming a standard deviation of 8–10 µm, with 80% statistical power and a significance level of 0.05, a minimum of 25 eyes per group was required. We included 30 eyes in each group to account for potential variability and improve study reliability.
- PXF group: 30 eyes with clinically diagnosed Pseudoexfoliation without glaucoma.
- Control group: 30 age-matched healthy eyes.

All participants were aged >40 years and had no history of glaucomatous visual field defects. The study was approved by the institutional ethics committee, and written informed consent was obtained from all participants.

Inclusion criteria

- Age >40 years
- Clinically diagnosed Pseudoexfoliation, confirmed by slit-lamp examination of the anterior segment
- Absence of glaucomatous visual field defects on Zeiss HFA 24-2 SITA Standard programme Clear ocular media sufficient for reliable SD-OCT imaging

Exclusion criteria

- History of ocular trauma or intraocular surgery
- Other optic neuropathies or retinal diseases (e.g., optic neuritis, retinal vein occlusion, macular pathology)
- Systemic diseases known to affect the optic nerve (e.g., advanced diabetic optic neuropathy, severe anemia, systemic vasculitis)
- Previous or current use of medications that may significantly alter RNFL measurements (e.g., optic nerve-toxic drugs)

Ophthalmic examination

-IOP measurement: Goldmann applanation tonometry, with three readings averaged for each eye.
- RNFL assessment: Peripapillary RNFL thickness was measured using Zeiss Primus 200 SD OCT. The instrument recorded average RNFL thickness and quadrant-specific values (superior, inferior, nasal, temporal) around the optic disc.

Statistical analysis

Statistical analysis was performed using SPSS version 20. Continuous variables are presented as mean ± standard deviation. Independent t-tests were used to compare mean RNFL values between the Pseudoexfoliation and control groups. A p value < 0.05 was considered statistically significant.

RESULTS

Baseline demographic and IOP parameters were comparable between groups; mean age and IOP did not differ significantly ($p > 0.05$).
Peripapillary RNFL thickness values are summarized in Table 1.

Table 1: Peripapillary RNFL thickness in Pseudoexfoliation versus controls

Parameter	PXF group (µm)	Control group (µm)	p value
Mean RNFL thickness	76.9	84.2	0.016
Inferior quadrant RNFL	88.4	100.4	0.011
Superior quadrant RNFL	82.3	86.5	>0.05
Nasal quadrant RNFL	65.1	68.7	>0.05
Temporal quadrant RNFL	58.6	61.2	>0.05

Table 2; Age distribution

Age Group	PXF Count	Control Count
40-49	1	2
50-59	3	4
60-69	12	11
70-79	10	9
80+	4	4

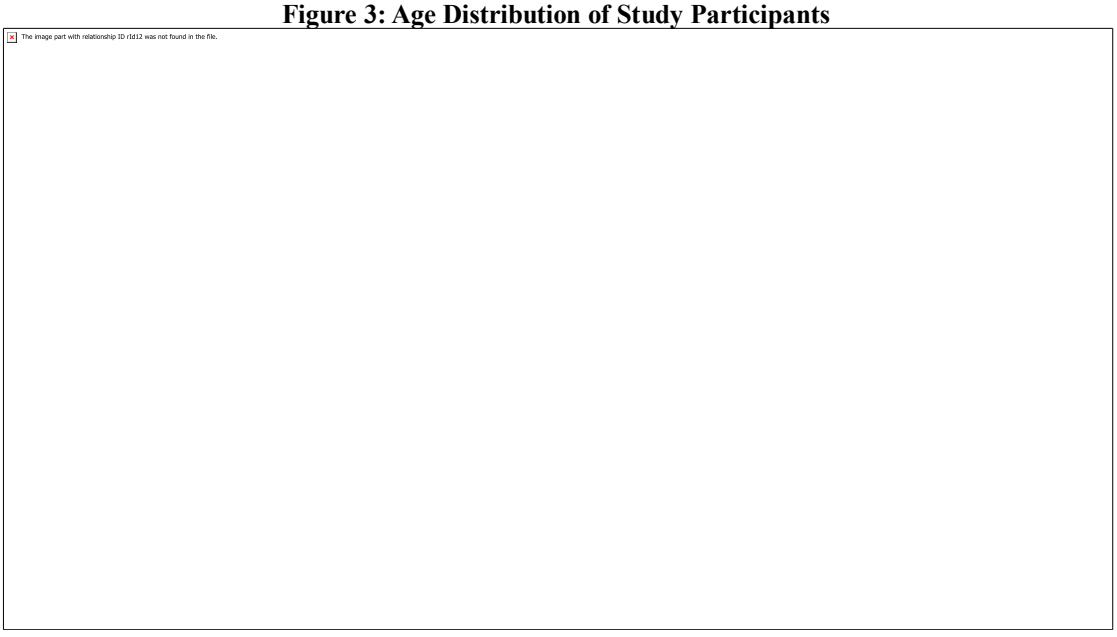
Mean RNFL thickness was significantly lower in Pseudoexfoliation eyes than in controls ($p = 0.016$). The inferior quadrant showed the most pronounced difference (88.4 µm vs 100.4 µm; $p = 0.011$). In contrast, neither superior, nasal, nor temporal quadrant thicknesses reached statistical significance (all $p > 0.05$).

These findings are consistent with prior reports, including the meta-analysis by Yu et al. (2017), which showed a mean RNFL reduction in PXF eyes, and the study by Yasmeen et al. (2016), which reported thinner average RNFL and significant inferior-quadrant loss in Pseudoexfoliation PXF eyes. [1, 2]

Figure 1: Quadrant-wise RNFL thickness (µm) in pseudoexfoliation syndrome (PXF) versus healthy controls. The inferior quadrant shows the largest difference between groups

Figure 2: Proportion of peripapillary RNFL quadrants demonstrating significant thinning in Pseudoexfoliation ($p < 0.05$) versus those not significantly different ($p \geq 0.05$) .

Figure 3: Age Distribution of Study Participants



DISCUSSION

This study confirms that patients with pseudoexfoliation syndrome, even in the absence of elevated IOP or glaucomatous visual field defects, exhibit significant RNFL thinning. The inferior quadrant emerges as the most consistently affected region, which may reflect early axonal vulnerability in this sector of the optic nerve head.[1-6,10,11]

Our results align closely with the 2017 meta-analysis by Yu et al., which demonstrated a mean RNFL reduction in Pseudoexfoliation eyes, with thinning across all quadrants. The smaller sample size of the present study likely limited statistical power for detecting significant differences in the superior, nasal, and temporal quadrants, despite the same directional trend.[1]

The findings also mirror those of Yasmeen et al., who reported thinner average RNFL and significant inferior quadrant thinning in a Pakistani cohort. Variations in absolute RNFL values across studies may be attributable to differences in age, ethnicity, OCT device, and normative databases, but the overall pattern of inferior-quadrant predominant involvement is consistent. [2-6,10]

Clinically, these observations underscore that Pseudoexfoliation is not merely an anterior segment finding but a condition associated with early structural optic nerve damage. Even when IOP and visual fields are within normal limits, RNFL thinning may already be present. Incorporating routine SD –OCT screening into the follow –up of Pseudoexfoliation patients can therefore help detect subclinical optic nerve involvement and allow earlier intervention before irreversible damage occurs.[1-6,10-12]

Limitations

-Small sample size (30 Pseudoexfoliation eyes).
-Cross-sectional design with no longitudinal follow-up.
-Single center setting, which may limit generalizability.
-No formal analysis of OCT device specific normative data or age-adjusted RNFL deviation maps.
Future studies should focus on larger, multi-center, longitudinal cohorts using standardized SD-OCT protocols to better characterize RNFL change rates and their association with progression to pseudoexfoliative glaucoma.[11,12]

CONCLUSION

RNFL thinning is a structural hallmark of pseudoexfoliation syndrome, occurring even in the absence of glaucoma. In this study, the inferior quadrant showed the most marked RNFL reduction, while the other quadrants did not differ significantly between groups. Our findings, together with evidence from meta-analysis and regional studies, support the use of routine SD-OCT screening in Pseudoexfoliation patients to facilitate early detection of optic nerve damage and preserve visual function.

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