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Central Corneal Thickness in Pseudoexfoliation Syndrome: A Comparative Study

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1. INTRODUCTION

As the population ages, prevalence of ocular disorders such as glaucoma, AMD(age-related macular degeneration), cataracts, and diabetic retinopathy increases significantly [1-3]. These conditions are major contributors to vision impairment and blindness among older adults. Among these, PXF(pseudoexfoliation syndrome) is common age-related condition marked by accumulation of fibrillar material on anterior segment of eye. PXF is notably a risk factor for cataracts as well as secondary glaucoma, necessitating a deeper understanding of its pathophysiology and implications for ocular health [4,5]. Pseudoexfoliation syndrome involves production as well as deposition of extracellular fibrillary material on several ocular structures, including the cornea, lens, and iris. The global prevalence of PXF is approximately 1%, increasing to 6% in individuals aged 80-89 years [6]. Regions such as Iceland and Finland report rates as high as 25-38%, while certain populations, like Greenland Eskimos, show no prevalence. In India, studies indicate a prevalence of about 5% among individuals aged 40 and older [7].

Age is a significant risk factor for PXF, with incidence rates rising dramatically after age 60. Research indicates that individuals with PXF have thinner central corneas compared to healthy counterparts, which can complicate intraocular pressure (IOP) assessments crucial for glaucoma diagnosis [8]. This study was aimed at comparing the CCT (central corneal thickness) between patients with healthy controls as well as PXF.

2. METHODOLOGY

This case-control study employed pachymetry and Goldmannapplanationtonometry to measure CCT and IOP in 95 patients diagnosed with PXF and 95 healthy controls, over a period of 18 months. Study excluded patients with any previous ocular injury, opacity, surgery, or with pre-existing glaucoma history. A detailed ophthalmic examination was conducted to ensure accurate diagnosis and exclusion of other ocular pathologies.

Materials and Methods

Study Subjects

Patients from the OPD of the Department of Ophthalmology, SSSMCRI

Study Design

Case-control study

Study Period

Duration: 18 months

Study Setting

Study Area: OPD of the Department of Ophthalmology, SSSMCRI, Ammapettai.

Inclusion Criteria

• **Case-** all patients with PXF.

• **Control-** age-matched healthy individuals without pseudoexfoliation.

Exclusion Criteria

• previous ocular injury

• history of ocular surgeries

• corneal opacity

• pre-existing glaucoma

• corneal vascular disorders

• corneal ectasias

• corneal degeneration

• corneal dystrophies

• OHT

Ethical Considerations

The present study was performed after obtaining prior clearance from IEC (Institutional Ethical Committee). From each participant, written informed consent was acquired after clearly describing the purpose, procedure, potential risks as well as benefits of study in plain comprehensible language. Participant anonymity was maintained by removing their names and any other identification details from the data before analysis. The data once collected was coded to ensure maintenance data safety and confidentiality.

Study Procedure

Study Variables:

• patients age

• gender

• best corrected vision

• uncorrected vision

• visual fields

• IOP

• CCT

3. DATA COLLECTION

Research had been conducted on patients partitioned into 2groups. Patients with PXF were categorized as group1 (95 eyes with pseudoexfoliation) as well as healthy normal individuals without PXF as group2 (95 healthy eyes without pseudoexfoliation)

• Every patient who participated in study gave written informed consent.

• Slit-lamp biomicroscopy was used to examine anterior segment, moreover, Snellen's visual acuity chart was used to record

visual acuity.

• Examination of Visual Fields was done by automated perimetry (Humphrey's).

• Pachymetry was used to measure the central cornea thickness. At centre of the cornea, 5readings were taken in repeated sets until standard deviation of 5values was 5 µm or less.

• A Goldmannapplanation tonometer had been used to measure Intraocular pressure. Following pachymetry, corrected IOP had been measured.

• Dilated fundus examination had been conducted, as well as optic disc changes had been documented.

Data Analysis & Statistical Methods

Data was entered, cleaned and coded in Microsoft Excel 2010. Statistical analysis was done on Microsoft Excel and IBM SPSS version 21, using descriptive statistics and inferential statistics. The appropriate statistical tests were applied to test for significance of the findings, at5% level of significance and 95% confidence interval

This case-control study employed pachymetry, Goldmann applanation tonometry and automated perimetry (Humphrey's) to measure CCT, IOP and visual fields in 95 patients diagnosed with PXF and 95 healthy controls, over a period of 18 months. A detailed ophthalmic examination was conducted to ensure accurate diagnosis and exclusion of other ocular pathologies.

4. RESULTS

The present study enrolled 95 cases of pseudoexfoliation, and 95 age and gender-matched healthy controls. Mean age of case group was54.28±10.43years, and mean age of control group was54.11 ±9.03 years. Gender distribution showed higher proportions of females among the cases (49, 51.6%) as well as among the controls (52.6%), as compared to males (46, 48.4%, and 45, 47.4%, respectively). Tests of association showed 0significant differences in the gender as well as age characteristics of cases and controls.

Table 1: Comparison of mean age of the cases and controls.

	Cases (n=95)	**Controls (9=95)**	**t-test**
Mean age (in years)	54.28 ± 10.43	54.1 ± 19.03	0.900

Table 2: Gender distribution among the cases and controls

Gender	**Cases (n=95)**	**Controls (9=95)**	**Chi^2-test**
Male	**46 (48.4%)**	**45 (47.4%)**	**0.885**
Female	**49 (51.6%)**	**50 (52.6%)**	

Slit lamp examination showed that lids, conjunctiva and cornea were clear among all the cases as well as the controls. Pupils were rounded, regular and reactive to light among all the study subjects.The mean central corneal thickness was 510.37 ± 24.22 µm among the cases, whereas it was much higher among the controls, at 544.89 ± 8.78 µm. This difference was statistically significant, $t(118.29) = -13.06$, $p = <.001$.The mean intraocular pressures werehigher among the cases (RE: 21.56 ± 6.04 mm Hg, LE: 20.07 ± 5.17 mm Hg) as compared to the controls (RE: 14.33 ± 2.57 mm Hg, LE: 14.77 ± 2.90 mm Hg) in both the eyes (RE:p<0.001, and LE: p<0.001).Among the pseudoexfoliation cases, the mean CCT in males was 506 ± 28.83 µm and the mean CCT in females was 513.77 ± 18.58µm. However, this gender-based difference in CCT among cases was not statistically significant (p=0.079).

Regression analysis showed that the variable IOP-RE explained 46.77% of the variance from the variable CCT (in um) and the variable IOP-LE explained 27.42% of the variance from the variable CCT (in um). ANOVA tests showed that the effect was significantly different from zero in both eyes (RE: F=165.16, p = <0.001, $R^2 = 0.4$; LE: F=71.04, p = <0.001, $R^2 = 0.27$).

5. DISCUSSION

The present study delved into the ocular biomechanical changes associated with PXF, a common age-related eye condition. Pseudoexfoliationis characterized by fibrillar material accumulation in anterior segment of eye, often leading to secondary complications like glaucoma and cataract. The current study aimed to investigate PXF's impacton CCT as well as on IOP. By comparing a cohort of 95 pseudoexfoliationpatients with age- and gender-matched controls, the present study found significant differences in these ocular parameters.No gender predisposition had been shown in our study among

pseudoexfoliation cases.

In our study pachymetry had been used to measure CCT moreover findings showed that the mean CCT in pseudoexfoliation was lower in pseudoexfoliation as compared to that in normal controls. Among the pseudoexfoliation cases, the mean CCT in males was 506 ± 28.83 μmand the mean CCT in females was 513.77 ± 18.58μm. However, this gender-based difference in CCT among cases was not statistically significant (p=0.079).

Table 3: Mean CCT among the cases and controls.

	Cases (n=95)	**Controls (9=95)**	**t-test**
Mean Central Corneal Thickness (μm)	510.37 ± 24.22	544.89 ± 8.78	**<0.001**

Study done by Sharma M et al [10] reported that the mean CCT obtained from specular microscopy in pseudoexfoliation patients was487.34 ± 27.16μm however in normal controls it was 505.09 ± 26.36 μm. The present study confirmed previous findings [9-13] that pseudoexfoliationpatients have corneas significantly thinner on comparingwithhealthy individuals, aligning with the established association between pseudoexfoliationand alterations in corneal structure [9-13]. Another study by Kitsos et al [11] reported similar results using pachymetry.

The present study further reinforces the well-documented link between pseudoexfoliationand elevated IOP. The observed increase in IOP in pseudoexfoliationpatients is consistent with previous research [12,13,14], which has identified pseudoexfoliationas a major risk factor for secondary glaucoma.An older study by Zheng X et al [15] suggested that deposits of pseudoexfoliationmatured probably leading to apoptosis of stromalkeratocytes of cornea, which eventually leads to thinning of cornea, giving way to raised IOP.

The present study also demonstrated thinner corneas are associated with false low IOP, wherein the patients actually had glaucoma but the IOP wasn't as high as expected but rather barely above the normal ranges. This finding was in line with previous studies [12,13,14] that have highlighted the role of corneal biomechanics in IOP regulation.

There should be an emphasis on importance of early detection as well aspseudoexfoliation management for preventing glaucoma development as well as other vision-threatening complications. Because of misleadingly low IOP caused by decreased CCT, glaucoma often gets overlooked in affected patients, leadingto increased severity andultimately irreversible damage. Routine pachymetry is an essential investigation in all patients with pseudoexfoliation to avoid underestimating the value of the IOP. Ehler's algorithm is a useful tool for estimating the correct value of the IOP given the central corneal thickness, thereby avoiding the underestimation of the IOP. Regular eye examinations, particularly for individuals with a family history of pseudoexfoliation or those in high-risk age groups, are crucial for timely diagnosis and intervention. The present study thus indicates a promising future in investigating role of genetic factors in PXF or exploring long-term outcomes of different treatment approaches.To explore underlying pseudoexfoliation mechanisms and for developing novel therapeutic strategies to mitigate its impact on ocular health, further studies are required.

Table 4: Mean IOP in Right eye and in Left eye among the cases and controls.

	Cases (n=95)	**Controls (9=95)**	**t-test**
IOP-RE (mm Hg)	23.56 ± 8.04	14.33 ± 2.57	**<0.001**
IOP-LE (mm Hg)	20.07 ± 5.17	14.77 ± 2.9	**<0.001**

6. CONCLUSIONS

The present study demonstrated that patients with pseudoexfoliationexhibited reduced central corneal thickness compared to controls, suggesting alterations in ocular biomechanics. These patients also displayed an elevation inintraocular pressure, highlighting the increased risk of secondary glaucoma with pseudoexfoliation. The slight raise in IOPwas not commensurate with the significant visual field defects demonstrated by automated perimetry in these patients, indicating glaucoma. The decreased corneal thickness was giving a misleadingly low value of IOP (lower than the actual value). Hence caution must be exercised when encountering a normal or only a slightly elevated IOP in a patient with pseudoexfoliation. In such patients, CCT measurement and automated perimetry to check visual fields are a non-negotiable to rule out pseudoexfoliative glaucoma, which might otherwise be missed due to the misleading IOP value

7. ADVANTAGES

The robust case-control design of the present study allowed direct comparison between pseudoexfoliation cases and normal controls, while also minimizing the confounding effects of age and gender by taking age-matched and gender-matched

controls. The use of standardized methods such as ultrasonic pachymetry and Goldmanntonometry provided accurate CCT and IOP measurements.

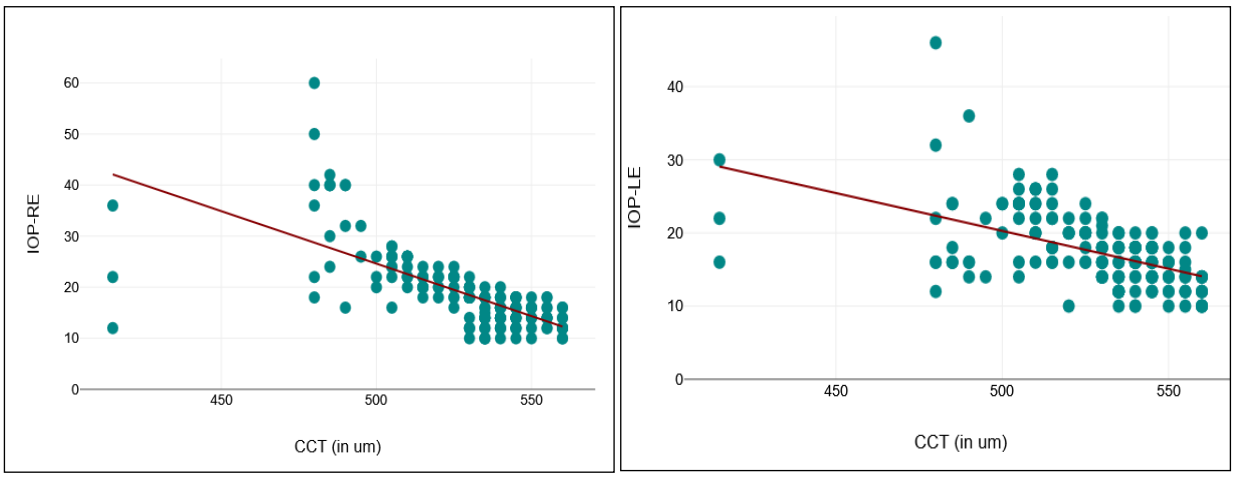

Figure 1: Scatter plots showing the correlation between CCT and IOP in RE and LE.

8. LIMITATIONS

This study has limited external validity of the findings due tobeing conducted at a single centre, among a small sample size owing to the restricted study period.

Inter-observer and intra-observer variability in measurement of IOP, lack genetic or biochemical analysis and lack of longitudinal follow-up could impact the reliability of the findings in this study.

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