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Research Article

Corneal Endothelial Changes in Senile Cataract: A Cross-Sectional Comparison between Patients with and Without Pseudo Exfoliation

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ABSTRACT
Background: Pseudo exfoliation syndrome (PXF) is an age-related systemic disorder characterized by the accumulation of fibrillar extracellular material on ocular structures such as the lens capsule, iris, and corneal endothelium. Its coexistence with senile cataract has significant surgical and prognostic implications, as pseudoexfoliative deposits can lead to endothelial cell damage, decreased cell density, and morphological alterations, thereby increasing the risk of intraoperative and postoperative complications.
Aim: To evaluate and compare the corneal endothelial cell density and morphology using specular microscopy in senile cataract patients with and without pseudo exfoliation syndrome.
Materials and Methods: A cross-sectional study was conducted in the Department of Ophthalmology, Narayana Medical College, Nellore, including 160 patients diagnosed with senile cataract. Among them, 80 patients had PXF and 80 age-matched controls did not. All subjects underwent a detailed ophthalmic evaluation, including best-corrected visual acuity (BCVA), intraocular pressure (IOP) measurement, and corneal endothelial assessment using specular microscopy. Quantitative parameters studied included endothelial cell density (ECD), coefficient of variation (CV%), hexagonality (6A%), and central corneal thickness (CCT).
Results: The majority of patients were above 60 years of age with nearly equal gender distribution. Patients with PXF exhibited a significantly lower mean ECD (1986.20 ± 954.41 cells/mm²) compared to those without PXF (2891.81 ± 134.65 cells/mm²). The mean CV% was higher (51.10 ± 46.11% vs. 31.25 ± 1.18%), and the mean hexagonality lower (39.99 ± 7.44% vs. 44.18 ± 3.98%) in the PXF group. Mean CCT was also reduced in PXF patients (389.02 ± 25.14 µm vs. 513.02 ± 31.43 µm), indicating significant endothelial cell loss, increased pleomorphism, and corneal thinning.
Conclusion: pseudo exfoliation is associated with significant endothelial degeneration and morphological changes that progress with age. Careful preoperative evaluation and surgical planning are crucial in these patients to prevent corneal endothelial decompensation.

Keywords: Pseudo Exfoliation Syndrome, Senile Cataract, Corneal Endothelium, Specular Microscopy, Endothelial Cell Density, Central Corneal Thickness, Polymegathism, Pleomorphism.

INTRODUCTION

Pseudo exfoliation syndrome (PXF) is a systemic, age-related disorder first described by Lindberg in 1917. [1] It is characterized by progressive deposition of fibrillar extracellular material on anterior segment structures, including the lens capsule, iris, zonules, trabecular meshwork, ciliary body, and corneal endothelium.[2]The pseudoexfoliative material, appearing as greyish-white flaky deposits, is composed of abnormal basement membrane proteins and microfibrillar components. Although primarily ocular, PXF has systemic implications, affecting organs such as the skin, heart, and kidneys. [3] Clinically, PXF is associated with keratopathy, cataract, glaucoma, pseudo uveitis, and zonular instability. [4]

The corneal endothelium is a non-regenerative monolayer of hexagonal cells essential for maintaining corneal transparency and deturgescence throughout life. [5] A normal adult cornea has an endothelial cell density (ECD) of approximately 2500 cells/mm², and when this falls below 800 cells/mm², corneal decompensation with stromal edema occurs, leading to impaired vision. [6] In PXF, chronic deposition of fibrillar material accelerates endothelial cell loss, resulting in secondary degeneration and asymmetric, slowly progressive corneal endotheliopathy. [7]

Recent studies using specular microscopy confirm that eyes with PXF exhibit significantly lower ECD (~2212 ± 312 cells/mm² vs ~2588 ± 286 in controls), higher average cell area, reduced hexagonality, and increased coefficient

of variation, indicating polymegathism and pleomorphism. [8,9] Central corneal thickness (CCT) is often thinner in PXF eyes, which can result in underestimation of intraocular pressure (IOP), a critical issue given the higher susceptibility of PXF eyes to glaucomatous optic nerve damage. [10]

Cataract surgery in PXF patients carries increased intraoperative risk due to zonular weakness, poor pupillary dilation, and fragile capsules, predisposing to posterior capsule rupture, vitreous loss, and lens subluxation. [11] Systematic reviews and cohort studies indicate up to a fivefold higher complication rate in PXF eyes compared to non-PXF eyes, highlighting the necessity of meticulous preoperative assessment and careful surgical planning. [12,13]

Specular microscopy is a vital non-invasive tool for evaluating corneal endothelial health. It captures reflected light from the corneal interface and provides detailed quantitative analysis of endothelial density, morphology, and cell size variability. [14] Recent studies from India and Syria confirm that PXF is associated with lower ECD, increased polymegathism, reduced hexagonality, and thinner CCT, underlining its clinical relevance for preoperative assessment, risk stratification, and surgical planning in cataract patients. [15]

MATERIALS AND METHODS

Study Design and Setting

A cross-sectional study was conducted in the Department of Ophthalmology, Narayana Medical College, Nellore, between February 2025 and August 2025. The study included 160 eyes—80 eyes of patients diagnosed with senile cataract and pseudo exfoliation (PXF) and 80 age-matched eyes of patients with senile cataract but without pseudo exfoliation. Participants were selected sequentially from the Outpatient and Inpatient Departments (OPD/IPD).

All participants provided written informed consent after being informed of the study objectives and procedures. The study protocol was reviewed and approved by the Institutional Ethics and Research Committee of Narayana Medical College.

Sample Size Calculation

The sample size was calculated using the formula for comparing two means:

n=2(Zα/2+Zβ)2σ2d2n = \frac{2 (Z_{\alpha/2} + Z_{\beta})^2 \sigma^2}{d^2}n=d22(Zα/2+Zβ)2σ2

Where:

- nnn = required sample size per group
- Zα/2Z_{\alpha/2}Zα/2 = standard normal deviate corresponding to the desired confidence level (1.96 for 95% confidence)
- ZβZ_{\beta}Zβ = standard normal deviate corresponding to desired power (0.84 for 80% power)
- σ\sigmaσ = standard deviation from previous studies
- ddd = expected mean difference between the two groups

Based on similar studies assessing endothelial cell count differences between pseudoexfoliation and non-pseudoexfoliation cataract patients ($\sigma \approx 300$ cells/mm²; expected difference $d \approx 150$ cells/mm²), the minimum sample size per group was calculated as approximately 72 eyes. To enhance study validity and account for possible data loss, the sample size was rounded up to 80 eyes per group, totaling 160 eyes.

Study Population

- Group I: 80 eyes with senile cataract and pseudoexfoliation
- Group II: 80 eyes with senile cataract without pseudoexfoliation

Inclusion Criteria

- Patients aged ≥50 years with senile cataract
- Patients aged ≥50 years with senile cataract and pseudoexfoliation

Exclusion Criteria

- Traumatic, congenital, developmental, or complicated cataracts
- Eyes with corneal pathology or dry eye syndrome
- History of ocular surgery

Study Procedure

All patients underwent detailed ocular and systemic evaluation.

1. **Visual and Ocular Examination:**
    - Best-Corrected Visual Acuity (BCVA): Using Snellen's chart
    - Intraocular Pressure (IOP): Measured with Goldmann applanation tonometer
    - Anterior Segment and Fundus Examination: Using Appaswamy slit lamp biomicroscope
    - Detection of Pseudoexfoliative Material: At pupillary margin, anterior lens capsule, and anterior chamber angle

- Iridopathy: Examined for stromal atrophy, radial lines, or granular deposits

2. **Gonioscopy:**
Conducted using a handheld four-mirror indirect gonioscope under topical anesthesia (4% xylocaine). The Shaffer Grading System was used for angle evaluation

Table : Shaffer Grading System

Grade	Angle Width	Description	Risk of Closure
4	45–35°	Wide open	Impossible
3	35–20°	Wide open	Impossible
2	20°	Narrow	Possible
1	<10°	Extremely narrow	Probable
Slit	Narrowed to slit	Probable	
0	Closed	Closed	

Intraocular Pressure Correction
The corrected intraocular pressure (IOP) was calculated based on central corneal thickness (CCT) using the Ehlers et al. formula:
Corrected IOP=Measured IOP+5×(Mean Norm al CCT−Measured CCT)70\text{Corrected IOP} = \text{Measured IOP} + \frac{5 × (\text{Mean Normal CCT} - \text{Measured CCT})}{70}Corrected IOP=Measured IOP+705 ×(Mean Normal CCT−Measured CCT)

The corresponding adjustment values used in the study are shown in below Table .

Table : CCT-Based IOP Adjustment

Central Corneal Thickness (µm)	Adjustment in IOP (mmHg)
445	+7
475	+5
505	+3
545	0
575	-2
605	-4
635	-6
645	-7

Grading of Pseudoexfoliation
After pupillary dilation with tropicamide (0.8%) and phenylephrine (5%), one drop was instilled every 10 minutes over a 30-minute period. The deposition of pseudoexfoliative material was graded as follows.

Table : Grading of Pseudoexfoliation

Grade	Description
I (Mild)	Exfoliation confined to lens periphery; visible only after dilation
II (Moderate)	Flakes of exfoliated material on iris edge and/or lens capsule
III (Severe)	Flakes visible in the angle or on posterior corneal surface

Specular Microscopy
Endothelial cell analysis was performed using a Tomey SP-3000P non-contact specular microscope. Participants were instructed to fixate on a red target while a bright central specular image of the corneal endothelium was captured. Up to 300 endothelial cells were analyzed per image (covering an area of 0.135 mm²).

Parameters Recorded
- Endothelial Cell Density (ECD) – cells/mm²
- Coefficient of Variation (CV) – variation in cell size
- Percentage of Hexagonal Cells – measure of cell shape uniformity
- Central Corneal Thickness (CCT)

Statistical Analysis
All data were entered and analyzed using Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA) and GraphPad Prism version 6.0 (GraphPad Software, San Diego, CA, USA).

Data were initially checked for completeness and consistency. Continuous variables such as endothelial cell density (ECD), central corneal thickness (CCT), percentage of hexagonal cells, and coefficient of variation (CV) were summarized as mean ± standard deviation (SD), while categorical variables such as sex and pseudoexfoliation grade were expressed as frequencies and percentages.

The Shapiro–Wilk test was applied to assess the normality of data distribution. As data were found to be normally distributed, parametric tests were employed for analysis.

- Comparison between two groups (PXF vs. non-PXF cataract eyes) was performed using the Student's unpaired t-test.
- Intragroup comparisons, where applicable, were performed using the paired t-test.
- Categorical variables were analyzed using the Chi-square test or Fisher's exact test (when cell counts were <5).

A p-value ≤ 0.05 was considered statistically significant, and a p-value < 0.01 was considered highly significant. All statistical tests were two-tailed.

RESULTS

A total of 160 patients with senile cataract were examined, comprising 82 males (51.25%) and 78 females (48.75%), indicating a nearly equal gender distribution. The majority of patients (66.9%) were aged between 60 and 79 years, with a slight predominance of right-eye involvement (60%). Senile mature cataract was the most frequent type (70%), and 35% of patients had associated systemic illnesses—most commonly diabetes and hypertension.The study population was predominantly elderly with a balanced gender ratio. Right-eye involvement was slightly more common, and mature cataract constituted the majority of cases.

Table 1. Demographic and Clinical Characteristics of the Study Population (n = 160)

Parameter	Category	Frequency (n)	Percentage (%)
Gender	**Male**	82	51.25
	Female	78	48.75
Age Group (years)	50–59	21	13.13
	60–69	58	36.25
	70–79	49	30.62
	≥80	32	20.00
Eye Involved	Right	96	60.00
	Left	64	40.00
Type of Cataract	Senile Immature (SIMC)	36	22.50
	Senile Mature (SMC)	112	70.00
	Senile Hypermature (SHMC)	12	7.50
Systemic Illness	None	104	65.00
	Diabetes Mellitus	12	7.50
	Hypertension	15	9.37
	DM + HTN	20	12.50
	Others (BA, IHD)	9	5.63

Table 2. Comparison of Corneal Endothelial Parameters in Patients with and Without Pseudo exfoliation (PXF)

Parameter	With PXF (Mean ± SD)	Without PXF (Mean ± SD)
Endothelial Cell Density (cells/mm²)	1986.20 ± 954.41	2891.81 ± 134.65
Coefficient of Variation (CV%, Polymegathism)	51.10 ± 46.11	31.25 ± 1.18
Hexagonality (% of Hexagonal Cells)	39.99 ± 7.44	44.18 ± 3.98
Central Corneal Thickness (µm)	389.02 ± 25.14	513.02 ± 31.43

PXF patients showed significantly lower mean ECD, higher CV%, and reduced hexagonality compared with non-PXF patients, indicating greater endothelial cell loss and morphologic

irregularity. Central corneal thickness was also thinner in the PXF group, suggesting corneal structural compromise.

Table 3. Age-Wise Distribution of Endothelial Cell Density (ECD) in Patients with and Without Pseudoexfoliation

Age Group (years)	With PXF (Mean ± SD)	Without PXF (Mean ± SD)
50–59	2231.11 ± 479.31	2574.12 ± 195.43
60–69	2348.36 ± 392.47	2712.45 ± 168.43
70–79	2230.84 ± 300.00	2644.00 ± 181.43
≥80	1211.18 ± 225.62	2879.50 ± 99.62

Across all age groups, patients with pseudoexfoliation had markedly lower endothelial cell counts than those without. The difference was most pronounced in the ≥80 years age group, reflecting the additive impact of age and pseudoexfoliation on endothelial degeneration.

Table 4. Fundus Findings in Study Participants

Fundus Finding	Frequency (n)	Percentage (%)
Within Normal Limits (WNL)	35	22.0
No View (Dense Cataract/Media Opacity)	119	74.4
Glaucomatous Changes	6	4.0

Due to dense cataract, fundus visualization was not possible in 74.4% of eyes. Glaucomatous changes were observed in 4% of patients, emphasizing the need for careful preoperative evaluation in pseudoexfoliation cases.

DISCUSSION

Pseudoexfoliation syndrome (PXS) is a systemic condition characterized by the accumulation of extracellular fibrillar material on ocular structures, including the corneal endothelium. This accumulation can lead to endothelial cell loss, resulting in decreased endothelial cell density (ECD). Studies have consistently demonstrated that eyes with PXS exhibit significantly lower ECD compared to age-matched controls without PXS. For instance, a study by Wang X et al. [16] found that ECD in PXS eyes was statistically significantly lower than in the control group. Similarly, Aoki et al. [17] reported a mean ECD of 2,548 ± 409 cells/mm² in the PXS group, which was significantly lower than the control group at 2,757 ± 282 cells/mm².

The coefficient of variation (CV) in endothelial cell area is another important parameter in assessing corneal endothelial health. A higher CV indicates greater pleomorphism and polymegathism, which are indicative of endothelial cell stress and potential decompensation. In a study by Javagal A et al., [18] the CV was significantly higher in PXS eyes compared to controls, suggesting increased endothelial cell variability and potential for decompensation.

Central corneal thickness (CCT) measurements also provide valuable information regarding corneal health. However, studies have shown conflicting results regarding CCT in PXS eyes. For example, Badran S,et al. [19] found that corneas in PXS patients were thinner compared to normals, with a mean CCT of 546.6 ± 39.6 µm in PXS patients versus 542.9 ± 32.2 µm in normals, though the difference was not statistically significant (p=0.56). In contrast, Patel DJ, et al. [20] reported that the CCT in PXS eyes was thicker than in normal eyes, with a mean CCT of 528 ± 30 µm in PXS eyes compared to 523 ± 32 µm in normal eyes, and this difference was statistically significant (p=0.01).

The morphological changes in the corneal endothelium associated with PXS, such as reduced ECD, increased CV, and altered CCT, have significant implications for intraocular surgeries, particularly cataract surgery. Decreased ECD and increased CV are risk factors for postoperative corneal decompensation. Therefore, it is crucial to assess these parameters preoperatively in patients with PXS to anticipate potential complications and plan surgical interventions accordingly.

In conclusion, Pseudo exfoliation syndrome (PXS) is a well-recognized risk factor for intraoperative and postoperative complications

in cataract surgery due to its adverse effects on ocular structures, including the corneal endothelium. The present study provides new quantitative evidence demonstrating that PXS is associated with significantly reduced corneal endothelial cell density, increased polymegathism and pleomorphism, and thinner central corneas compared to non-PXF cataract eyes. These findings highlight the extent of endothelial compromise in PXS and emphasize the importance of comprehensive preoperative evaluation of corneal endothelial health and central corneal thickness to minimize surgical risks and achieve optimal postoperative outcomes.

Limitations of the Study

The study was conducted at a single tertiary care centre, limiting generalizability to the wider population.

The cross-sectional design prevented evaluation of longitudinal endothelial changes over time.

A relatively small, non-randomized sample may have introduced selection bias.

Specular microscopy measurements were operator-dependent and subject to image quality variations.

Exclusion of patients with other ocular conditions limits the applicability of results to mixed-pathology populations.

Postoperative or long-term endothelial assessments were not included in the study design.

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