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Original Article

Corneal Endothelial Alterations in Senile Cataract with and Without Pseudoexfoliation: A Comparative Specular Microscopy Study

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ABSTRACT

Background; Pseudoexfoliation syndrome (PXF) is an age-related systemic microfibrillopathy characterized by the deposition of fibrillar extracellular material in ocular tissues. It is associated with endothelial dysfunction, increased intraoperative complications during cataract surgery, and a higher risk of corneal decompensation. Evaluation of corneal endothelial status using specular microscopy is therefore crucial in patients with PXF.

Objective; To evaluate and compare corneal endothelial cell density (ECD) and endothelial morphology using specular microscopy in senile cataract patients with and without pseudoexfoliation.

Methods; This prospective, comparative study was conducted at Department of Ophthalmology, Andhra Medical College, Visakhapatnam, from January 2025 to January 2026. A total of 100 patients with senile cataract were included: 50 patients with pseudoexfoliation (PXF group) and 50 age-matched patients without pseudoexfoliation (control group). All patients underwent comprehensive ophthalmic evaluation including slit-lamp examination, intraocular pressure measurement, gonioscopy, and non-contact specular microscopy (Tomey EM-3000). Endothelial cell density (cells/mm²), coefficient of variation (CV%) indicating polymegathism, percentage of hexagonal cells (6A) indicating pleomorphism, and central corneal thickness (CCT) were recorded. Statistical analysis was performed using SPSS software; $p < 0.05$ was considered statistically significant.

Results; The mean endothelial cell density was significantly lower in the PXF group (2180.20 ± 404.41 cells/mm²) compared to the control group (2695.86 ± 124.94 cells/mm²) ($p < 0.0001$).

The mean coefficient of variation was higher in patients with PXF (40.90 ± 8.69) compared to controls (37.70 ± 3.99), indicating increased polymegathism.

The mean percentage of hexagonal cells was significantly reduced in the PXF group (40.20 ± 5.44) compared to the control group (44.18 ± 3.98) ($p < 0.001$), demonstrating increased pleomorphism.

Central corneal thickness was significantly lower in the PXF group (489.02 ± 25.14 µm) compared to controls (513.02 ± 31.43 µm).

These findings indicate significant quantitative and qualitative endothelial alterations in patients with pseudoexfoliation.

Conclusion; Senile cataract patients with pseudoexfoliation demonstrate significantly reduced endothelial cell density, decreased central corneal thickness, and altered endothelial morphology characterized by polymegathism and pleomorphism. Preoperative assessment with specular microscopy is essential in PXF patients to identify those at higher risk of corneal decompensation and to plan appropriate surgical strategies. Careful endothelial evaluation should be considered a mandatory preoperative step in cataract patients with pseudoexfoliation.

***Keywords**: Pseudoexfoliation syndrome; Endothelial cell density; Specular microscopy; Corneal endothelium; Polymegathism; Pleomorphism; Central corneal thickness.*

INTRODUCTION

Pseudoexfoliation syndrome (PEX), first described by Lindberg in 1917, is an age-related systemic microfibrillopathy characterized by progressive accumulation of abnormal fibrillar extracellular material in ocular tissues [1]. It has a strong genetic association, particularly with polymorphisms in the lysyl oxidase-like 1 (LOXL1) gene [2]. Pseudoexfoliative material is deposited on anterior segment structures including the trabecular meshwork, lens capsule, iris, ciliary body, and corneal endothelium, and is clinically associated with senile cataract, secondary open-angle glaucoma, zonular instability, and keratopathy [3,4]. The coexistence of cataract and PEX is common in elderly patients, making its recognition crucial in routine cataract practice.

The corneal endothelium is a monolayer of hexagonal cells responsible for maintaining corneal transparency through barrier and metabolic pump functions [5]. In healthy adults, endothelial cell density (ECD) ranges between 2500–3000 cells/mm² and declines at an average rate of approximately 0.6% per year [6]. When ECD falls below a critical threshold, corneal deturgescence fails, leading to stromal edema and visual impairment. Several studies have demonstrated reduced endothelial cell density and morphological alterations such as polymegathism and pleomorphism in pseudoexfoliative eyes, predisposing them to endothelial decompensation, particularly following intraocular surgery [7,8]. Central corneal thickness (CCT) may also be altered in PEX, and variations in CCT can influence intraocular pressure (IOP) measurements, potentially leading to underestimation of glaucomatous risk [9]. These factors assume greater clinical importance because pseudoexfoliative eyes have an increased incidence of intraoperative complications during cataract surgery due to zonular weakness and poor pupillary dilation [10].

Despite available literature, several lacunae remain. Many previous studies evaluated endothelial changes in PEX without specifically focusing on senile cataract patients. Some investigations included small sample sizes, lacked age-matched controls, or assessed only endothelial cell density without comprehensive morphometric evaluation. Few studies have simultaneously analyzed endothelial cell density, coefficient of variation, hexagonality, and central corneal thickness in a single cohort [7,8]. Furthermore, data from the Indian population remain limited despite the high burden of cataract surgery.

The rationale of the present study is that comprehensive preoperative evaluation of endothelial parameters in pseudoexfoliative cataract patients may help identify individuals at higher risk of corneal decompensation and surgical complications. Therefore, the purpose of this study is to evaluate and compare corneal endothelial cell density, morphology, and central corneal thickness using specular microscopy in senile cataract patients with and without pseudoexfoliation.

MATERIALS AND METHODS

Study Design and Setting

This prospective comparative study was conducted in the Department of Ophthalmology, Andhra Medical College, Visakhapatnam, from January 2025 to January 2026.

Study Population

A total of 100 patients diagnosed with senile cataract and scheduled for cataract surgery were included in the study. The study group consisted of 50 patients with senile cataract associated with pseudoexfoliation (PXF group), and the control group consisted of 50 age-matched patients with senile cataract without pseudoexfoliation.

The study was approved by the Institutional Research and Ethics Committee of Andhra Medical College, Visakhapatnam. Written informed consent was obtained from all participants after explaining the nature and purpose of the study.

Inclusion Criteria

- Patients diagnosed with senile cataract
- Patients with senile cataract associated with pseudoexfoliation
- Patients willing to provide written informed consent

Exclusion Criteria

- Traumatic, congenital, developmental, or complicated cataract
- Eyes with corneal pathology
- Dry eye syndrome
- History of previous ocular surgery
- Patients unwilling to participate

Preoperative Evaluation
All patients underwent comprehensive preoperative evaluation including:
- Recording of demographic details (age, sex, occupation)
- Detailed medical and ophthalmic history
- Best corrected visual acuity (BCVA) using Snellen's chart
- Slit-lamp biomicroscopy for anterior segment evaluation
- Documentation of pseudoexfoliative material on the pupillary margin and anterior lens capsule
- Lacrimal syringing
- Intraocular lens (IOL) power calculation
- Posterior segment evaluation

Intraocular Pressure and Gonioscopy
Intraocular pressure (IOP) was measured using Goldmann applanation tonometry. Corrected IOP was calculated using Ehlers' formula:
Corrected IOP=Measured IOP+5(Mean normal CCT−Measured CCT)70Corrected\ IOP = Measured\ IOP + \frac{5 (Mean\ normal\ CCT - Measured\ CCT)}{70}Corrected IOP=Measured IOP+705(Mean normal CCT−Measured CCT)
Gonioscopy was performed under topical anesthesia (4% xylocaine) using a four-mirror indirect gonioscope. The following were specifically evaluated:
- Presence of excessive trabecular meshwork pigmentation
- Presence of pseudoexfoliative material in the angle
- Presence of Sampaolesi's line

Angle grading was done using the Shaffer grading system.

Pupil Dilatation and PXF Grading
Pupillary dilatation was achieved using topical tropicamide and phenylephrine, instilled every 10 minutes over 30 minutes. Slit-lamp examination was repeated to evaluate central and peripheral deposition of pseudoexfoliative material. Pseudoexfoliation was graded clinically based on severity.

Specular Microscopy
Non-contact specular microscopy was performed using the Tomey EM-3000 specular microscope. Patients were positioned with chin and forehead support and instructed to fixate on a central target. After proper alignment, a central endothelial image was captured.

Up to 300 endothelial cells were analyzed within a fixed area of 0.135 mm^2. Automated cell recognition software was used to assess:
- Endothelial cell density (ECD; cells/mm^2)
- Coefficient of variation (CV%) indicating polymegathism
- Percentage of hexagonal cells (6A) indicating pleomorphism
- Central corneal thickness (CCT)

The coefficient of variation was calculated as the standard deviation divided by the mean cell area.

Statistical Analysis
Data was entered into Microsoft Excel and analyzed using SPSS software version 18. Quantitative variables were expressed as mean ± standard deviation (SD). Categorical variables were presented as percentages and proportions. The unpaired t-test was used to compare quantitative variables between the two groups. A p-value < 0.05 was considered statistically significant.

RESULTS
A total of 100 patients with senile cataract were included in the study, comprising 50 patients with pseudoexfoliation (PXF group) and 50 age-matched controls.

1. Baseline Characteristics
The demographic characteristics of the study population are summarized in Table 1. The mean age in the PXF group was comparable to the control group, with no statistically significant difference. Females constituted a slightly higher proportion of the study population.

Table 1: Baseline Demographic Characteristics

Variable	PXF (n=50)	Control (n=50)	p-value
Age (years), Mean ± SD	66.84 ± 8.92	65.96 ± 8.47	0.62
Male, n (%)	22 (44%)	22 (44%)	1.00
Female, n (%)	28 (56%)	28 (56%)	1.00

(No significant demographic difference between groups.)

2. Clinical Characteristics

Senile immature cataract was the most common type in both groups. Pseudoexfoliative glaucoma was observed only in the PXF group.

Table 2: Clinical Characteristics

Variable	PXF (n=50)	Control (n=50)
Senile Immature Cataract	37 (74%)	37 (74%)
Senile Mature Cataract	9 (18%)	9 (18%)
Senile Hypermature Cataract	4 (8%)	4 (8%)
PEX Glaucoma	5 (10%)	0 (0%)

3. Endothelial Cell Density and Morphology

Comparison of endothelial parameters between the two groups is presented in Table 3.

The mean endothelial cell density (ECD) was significantly lower in the PXF group (2180.20 ± 404.41 cells/mm²) compared to the control group (2695.86 ± 124.94 cells/mm²). This difference was statistically highly significant ($p < 0.0001$).

The coefficient of variation (CV%) was higher in the PXF group; however, this difference was not statistically significant ($p = 0.07$).

The mean percentage of hexagonal cells (6A) was significantly reduced in the PXF group (40.20 ± 5.44) compared to controls (44.18 ± 3.98), and this difference was statistically significant ($p < 0.001$).

The mean central corneal thickness (CCT) was significantly lower in the PXF group (489.02 ± 25.14 µm) compared to controls (513.02 ± 31.43 µm), with statistical significance ($p < 0.001$).

Table 3: Comparison of Endothelial Parameters

Parameter	PXF (n=50) Mean ± SD	Control (n=50) Mean ± SD	p-value
Endothelial Cell Density (cells/mm²)	2180.20 ± 404.41	2695.86 ± 124.94	<0.0001
Coefficient of Variation (%)	40.90 ± 8.69	37.70 ± 3.99	0.07
Hexagonality (%)	40.20 ± 5.44	44.18 ± 3.98	<0.001
Central Corneal Thickness (µm)	489.02 ± 25.14	513.02 ± 31.43	<0.001

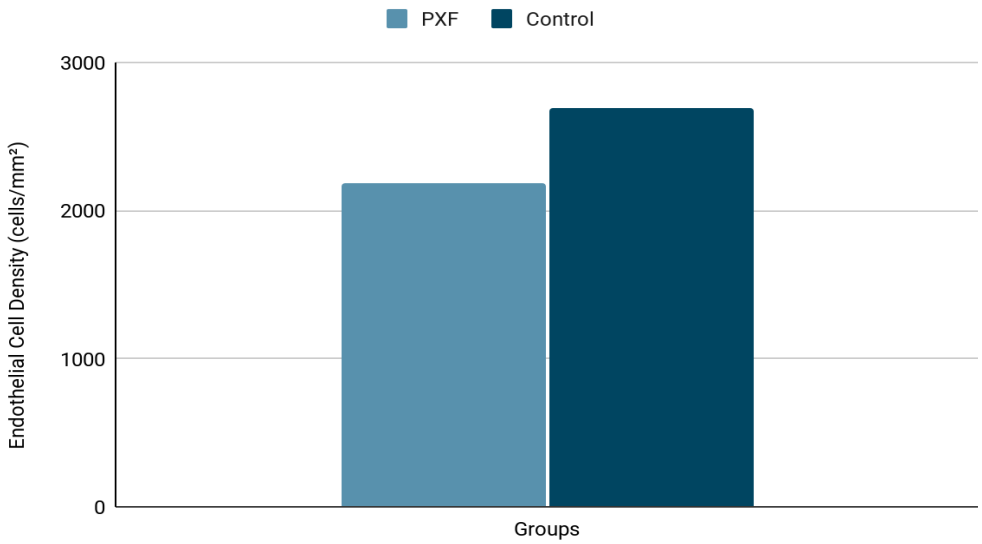

Figure 1: Mean Endothelial Cell Density Comparison

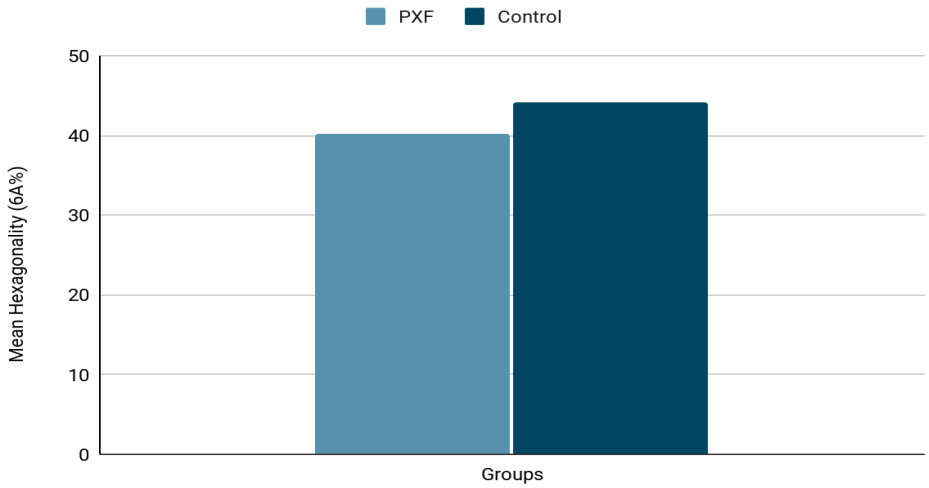

Figure 2: Mean Hexagonality (6A%) Comparison

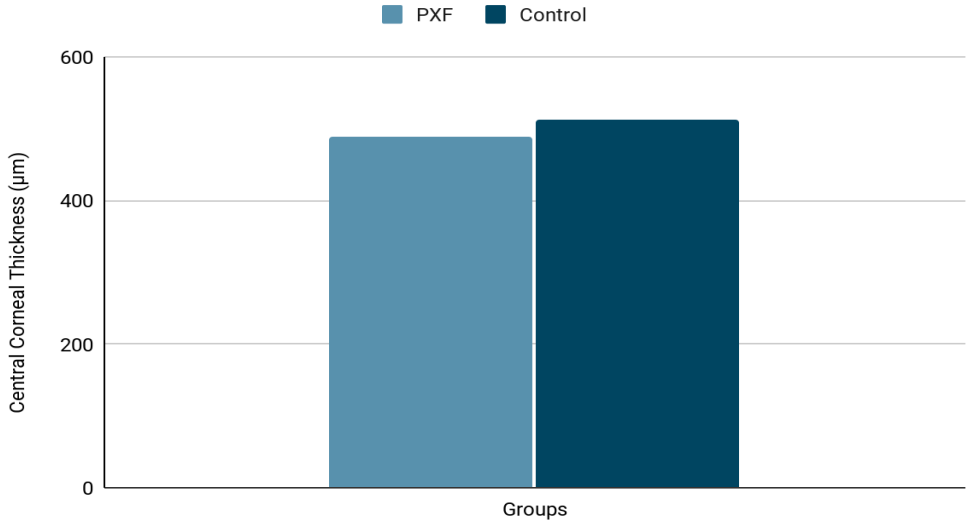

Figure 2: Mean Central Corneal Thickness (CCT)Comparison

4. Age-wise Endothelial Cell Density

Age-wise comparison demonstrated a progressive decline in endothelial cell density with advancing age in both groups. The reduction was more pronounced in patients aged ≥80 years in the PXF group.

Table 4: Age-wise Endothelial Cell Density

Age Group	PXF Mean ± SD	Control Mean ± SD	p-value
50–59	2159.18 ± 468.31	2674.12 ± 145.43	<0.01
60–69	2259.27 ± 383.60	2702.45 ± 120.43	<0.01
70–79	2190.14 ± 349.30	2734.00 ± 111.43	<0.01
≥80	1631.00 ± 218.75	2669.50 ± 94.62	<0.001

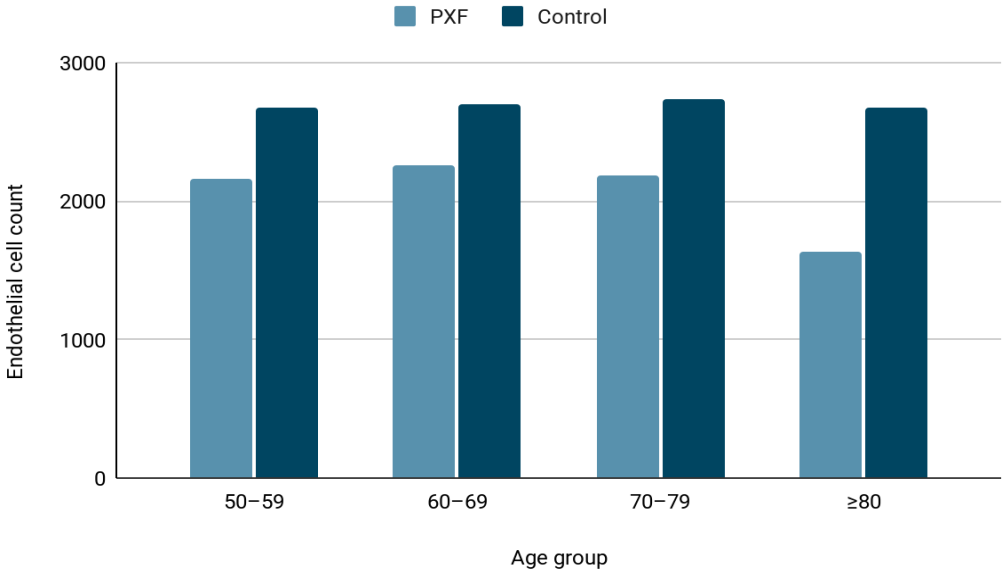

Figure 4: Age-wise Endothelial Cell Density

DISCUSSION

The corneal endothelium is a monolayer of hexagonal cells responsible for maintaining corneal transparency through its barrier and metabolic pump functions. Because human corneal endothelial cells have limited regenerative capacity, any cell loss is compensated by enlargement and redistribution of adjacent cells, leading to polymegathism and pleomorphism. Progressive endothelial loss beyond a critical threshold may result in corneal decompensation and visual impairment [11,12].

Pseudoexfoliation syndrome (PEX) is characterized by deposition of abnormal fibrillar extracellular material within anterior segment structures, including the corneal endothelium. Histopathological studies have demonstrated pseudoexfoliative material adherent to endothelial cells and Descemet's membrane, contributing to endothelial dysfunction [3,4,13]. Oxidative stress, anterior chamber hypoxia, increased transforming growth factor-β1 levels, and disruption of intercellular junctions have also been implicated in endothelial damage in PEX [14,15]. These mechanisms may accelerate endothelial apoptosis and structural compromise.

In the present study, the mean endothelial cell density (ECD) was significantly lower in the PXF group compared to controls ($p < 0.0001$). These findings are consistent with earlier studies by Zheng et al., Quiroga et al., and Kovliulas et al., who reported significant endothelial cell loss in pseudoexfoliative eyes [16–18]. Similar reductions in ECD have also been reported by Zarnowski et al. and Miyake et al., reinforcing the concept that PEX adversely affects endothelial reserve [7,19].

Morphological assessment in our study revealed a significant reduction in the percentage of hexagonal cells in the PXF group ($p < 0.001$), indicating increased pleomorphism. Although the coefficient of variation was higher in the PXF group, the difference was not statistically significant. These findings align with reports by Yuksel et al. and De Juan-Marcos et al., who demonstrated increased pleomorphism and polymegathism in pseudoexfoliative eyes, particularly in those with associated glaucoma [8,20]. Structural alterations of endothelial cells may precede overt cell loss and represent early endothelial compromise [21].

Central corneal thickness (CCT) was significantly lower in patients with pseudoexfoliation compared to controls ($p < 0.001$). Similar findings have been reported by Kitsos et al. and Acar et al., who observed thinner corneas in pseudoexfoliative eyes using ultrasonic pachymetry [22,23]. Reduced CCT may have important clinical implications, as thinner corneas can lead to underestimation of intraocular pressure, potentially delaying detection of pseudoexfoliative glaucoma [9,24].

Overall, the present study confirms that pseudoexfoliation is associated with significant quantitative and qualitative endothelial alterations. Reduced endothelial cell density and decreased hexagonality indicate compromised endothelial integrity, which may predispose these eyes to postoperative corneal edema following cataract surgery. Specular microscopic evaluation therefore plays a crucial role in preoperative risk stratification in patients with PEX [7,25].

Table 5: Comparison of Present Study with Previous Studies

Study	ECD in PXF (cells/mm²)	ECD in Control (cells/mm²)	CCT in PXF (µm)	CCT in Control (µm)
Zheng et al.	2105 ± 380	2568 ± 290	—	—
Quiroga et al.	2234 ± 415	2689 ± 305	—	—
Kovliulas et al.	2190 ± 402	2710 ± 280	—	—
Acar et al.	—	—	492 ± 28	515 ± 30
Kitsos et al.	—	—	490 ± 27	512 ± 25
Present Study	**2180.20 ± 404.41**	**2695.86 ± 124.94**	**489.02 ± 25.14**	**513.02 ± 31.43**

CONCLUSION

The present study demonstrates that senile cataract patients with pseudoexfoliation have significantly reduced endothelial cell density, decreased hexagonality, and thinner central corneal thickness compared with age-matched controls, indicating compromised endothelial integrity. These quantitative and qualitative endothelial alterations suggest a reduced endothelial reserve and a higher susceptibility to corneal decompensation following intraocular surgery. Additionally, decreased central corneal thickness in pseudoexfoliative eyes may lead to underestimation of intraocular pressure, potentially delaying recognition of glaucomatous damage. Therefore, preoperative evaluation of endothelial cell density, morphology, and central corneal thickness using specular microscopy is essential in cataract patients with pseudoexfoliation to facilitate appropriate surgical planning, minimize intraoperative and postoperative complications, and optimize visual outcomes.

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