RESEARCH PAPER

# Assessment Of Corneal Endothelial Changes In Patients With Pseudoexfoliation Syndrome Using Non Contact Specular Microscopy

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Abstract

**Background:**

Pseudoexfoliation syndrome (PEX) is an age-related systemic disorder characterized by deposition of abnormal fibrillar material in ocular tissues, particularly affecting the corneal endothelium. These changes can compromise endothelial function and increase the risk of complications during intraocular surgeries.

**Aim:**

To assess corneal endothelial changes in patients with pseudoexfoliation syndrome and compare them with age-matched normal individuals using non-contact specular microscopy.

**Materials and Methods:**

This comparative observational cross-sectional study was conducted over 18 months at a tertiary care centre at NIMS, Jaipur. A total of 104 participants (208 eyes) were included, comprising 52 patients with PEX syndrome and 52 age-matched controls. All subjects underwent detailed ophthalmological examination. Corneal endothelial parameters including endothelial cell density (ECD), coefficient of variation (CV), percentage of hexagonal cells (HEX), and central corneal thickness (CCT) were evaluated using a non-contact specular microscope.

**Results:**

The study revealed a significant reduction in endothelial cell density in PEX patients compared to controls. Increased coefficient of variation and decreased hexagonality were observed, indicating polymegathism and pleomorphism. These findings suggest structural and functional compromise of the corneal endothelium in PEX. Central corneal thickness showed variable changes between the groups. No statistically significant differences were observed in baseline demographic characteristics or intraocular pressure.

**Conclusion:**

Pseudoexfoliation syndrome is associated with significant corneal endothelial alterations. Non-contact specular microscopy serves as an effective, non-invasive tool for early detection. Routine endothelial assessment in PEX patients is essential for better surgical planning and improved clinical outcomes.

**Keywords:** Pseudoexfoliation syndrome, corneal endothelium, endothelial cell density, specular microscopy, central corneal thickness, polymegathism, pleomorphism, intraocular pressure

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## Introduction

Pseudoexfoliation syndrome (PXS) is an age-related systemic microfibrillopathy characterized by the production and progressive accumulation of abnormal extracellular fibrillar material in ocular and extraocular tissues. The condition predominantly affects the anterior segment of the eye and is recognized clinically by the deposition of gray-white material on the anterior lens capsule, pupillary margin, iris, trabecular meshwork, and corneal endothelium. PXS is considered the most common identifiable cause of secondary open-angle glaucoma worldwide and is associated with increased risks of cataract formation, zonular weakness, intraoperative complications, and postoperative corneal decompensation (1,2).

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The prevalence of PXS increases with advancing age and varies considerably among different populations because of genetic and environmental influences. Genetic studies have identified polymorphisms in the LOXL1 gene, which is involved in elastin metabolism and extracellular matrix remodeling, as major risk factors for the development of PXS (3).

In addition, oxidative stress, chronic inflammation, impaired blood-aqueous barrier function, and altered extracellular matrix metabolism contribute to disease pathogenesis (4).

The corneal endothelium is a monolayer of hexagonal, non-regenerating cells responsible for maintaining corneal deturgescence and transparency. Endothelial cell density (ECD) decreases physiologically with age; however, several pathological conditions accelerate endothelial loss. Because endothelial cells have minimal regenerative capacity, cell loss is compensated by enlargement and shape changes of adjacent cells, resulting in polymegethism and pleomorphism (5).

Pseudoexfoliative material has been demonstrated on the posterior corneal surface and within Descemet's membrane. Electron microscopic and histopathological studies have shown that pseudoexfoliative deposits directly affect endothelial cells, leading to decreased endothelial cell density, increased coefficient of variation, reduced hexagonality, and impaired endothelial function (6).

Elevated intraocular pressure and pseudoexfoliation glaucoma further aggravate endothelial damage through mechanical and ischemic mechanisms (7).

Several specular microscopy studies have demonstrated significantly lower endothelial cell density and greater morphologic abnormalities in eyes with PXS compared with age-matched controls. These changes are more pronounced in eyes with pseudoexfoliation glaucoma, suggesting that both pseudoexfoliative material and increased intraocular pressure contribute to endothelial deterioration (8,9).

Non-contact specular microscopy is a safe, rapid, and non-invasive technique for evaluating corneal endothelial morphology. It provides quantitative assessment of endothelial cell density, coefficient of variation, percentage of hexagonal cells, and central corneal thickness. These parameters are important for predicting endothelial reserve and assessing the risk of postoperative corneal complications, particularly in patients undergoing cataract or glaucoma surgery (10).

Because PXS eyes are more susceptible to endothelial damage and surgical trauma, preoperative endothelial assessment is essential. However, data regarding endothelial alterations in PXS patients, especially in Indian populations, remain limited. Therefore, the present study was undertaken to evaluate corneal endothelial changes in patients with pseudoexfoliation syndrome using non-contact specular microscopy and to compare these findings with age-matched controls.

**Aim**

Assessment of corneal endothelial changes in patients with pseudo exfoliation syndrome and to compare with normal population of the lens using specular microscopy.

**Objective**

To estimate:

1. Endothelial cell count,
2. Morphological characteristics and
3. Central corneal thickness in patients with pseudo exfoliation syndrome of the lens using Nidek (CEM-530) clinical specular microscope
4. To compare with normal population.

**Materials and Methods**

STUDY DESIGN: Comparative observational cross-sectional study

STUDY AREA: Department of Ophthalmology, National Institute of Medical Sciences and Research, Jaipur.

**INCLUSION CRITERIA FOR PSEUDOEXFOLIATION SYNDROME GROUP:**

1) Age : >/= 40 years of any sex
2) Patients diagnosed with pseudo exfoliation syndrome will be included.
3) Willing to participate in the study.

**INCLUSION CRITERIA FOR CONTROL GROUP:**

1) Age : >/= 40 years of any sex
2)Patients having no pseudoexfoliation syndrome.

EXCLUSION CRITERIA:

1) Subjects with any other ocular disease
2) Contact lens wearers
3) Past history of any intraocular surgery or laser treatment
4) Corneal dystrophies.

SAMPLE SIZE AND SAMPLING TECHNIQUE:

$$n = \frac{(Z_{\alpha/2} + Z_{1-\beta})^2 \times (\sigma_1^2 + \sigma_2^2)}{\Delta^2}$$

$$= \frac{1.96 \times 0.84)^2 \times (72.12^2 + 73.4^2)}{(40)^2} = 52$$

=52 samples/group

Where,

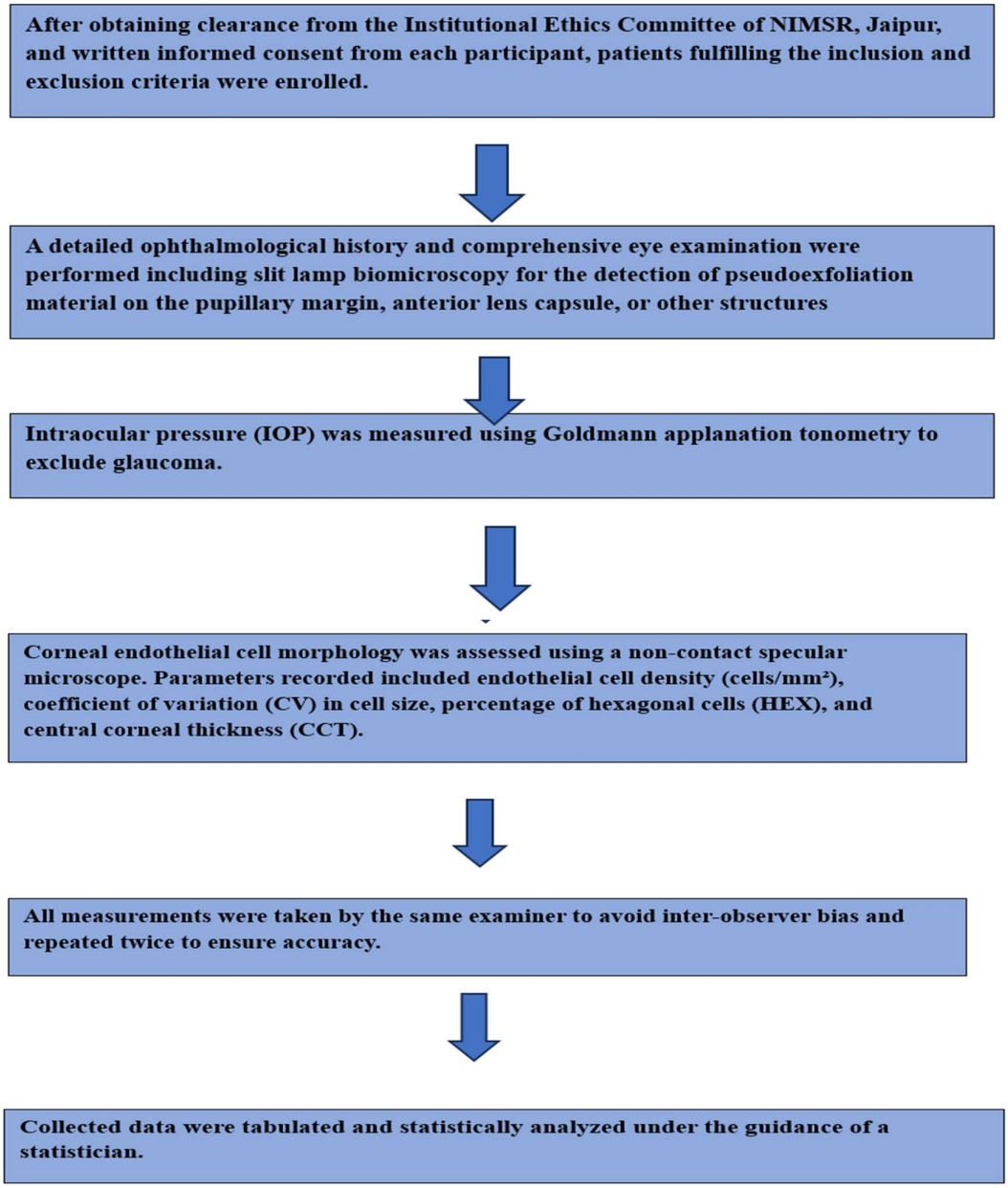
$Z_{\alpha/2}$ : Inverse probability of normal distribution at 95% confidence interval

$Z_{1-\beta}$ : Inverse probability of normal distribution at 80% power at the test

$\sigma_1$and $\sigma_2$ : Standard deviation of cell size of case and control group

D : Expected mean difference of cell size of case and control group

**METHODOLOGY**




**TECHNIQUE:**

- Diagnosis of pseudo exfoliation syndrome was made on slit lamp examination with and without mydriasis.
- A structured data collection sheet specially designed for the study was used.
- Non-contact specular microscopy (e.g., Topcon SP-3000P or equivalent) was employed to evaluate corneal endothelial parameters.
- Central corneal thickness was measured using the pachymetry function of the specular microscope.
- Intraocular pressure was measured using Goldmann applanation tonometer.

**Ethical Considerations**

The study was conducted in accordance with ethical standards. Written informed consent was obtained from all participants prior to inclusion in the study. Patient confidentiality was strictly maintained throughout the study.

**Results**

A total of 104 participants (208 eyes) were included in the study, comprising 52 patients with pseudoexfoliation syndrome (PEX group) and 52 age- and sex-matched healthy controls. The mean age of the PEX group was 59.77 ± 12.78 years, while that of the control group was 59.56 ± 13.10 years, with no statistically significant difference between groups (p = 0.934). Gender distribution was also comparable (p = 0.421). **Demographic Characteristics of Study Participants in Pseudoexfoliation (PEX) and Control Groups.**

| Variable | PEX Group (n=52) | Control Group (n=52) | p-value |
|---|---|---|---|
| Age (years), Mean ± SD | 59.77 ± 12.78 | 59.56 ± 13.10 | 0.934 |
| Male, n (%) | 22 (42.3%) | 26 (50.0%) | 0.421 |
| Female, n (%) | 30 (57.7%) | 26 (50.0%) | |

There were no significant differences in systemic or ocular baseline characteristics between the groups. Mean fasting blood sugar levels were 114.52 ± 34.79 mg/dL in the PEX group and 125.19 ± 41.37 mg/dL in controls (p = 0.146). Mean intraocular pressure was similar in both groups for the right eye (15.96 ± 1.72 mmHg vs 15.42 ± 1.63 mmHg; p = 0.092) and left eye (15.88 ± 1.64 mmHg vs 15.37 ± 1.59 mmHg; p = 0.108).

All patients in the PEX group demonstrated pseudoexfoliative deposits on the anterior lens capsule. Corneal endothelial analysis revealed significant alterations in PEX eyes compared with controls. The mean endothelial cell density (ECD) was significantly lower in PEX eyes in both the right eye (2368.35 ± 183.57 vs 2694.51 ± 118.79 cells/mm²; p < 0.001) and the left eye (2372.19 ± 190.44 vs 2689.76 ± 121.36 cells/mm²; p < 0.001).

**Comparison of Endothelial Cell Density (cells/mm²) Between PEX and Control Eyes.**

| Parameter | PEX Eyes | Control Eyes | p-value |
|---|---|---|---|
| RE ECD (Mean ± SD) | 2368.35 ± 183.57 | 2694.51 ± 118.79 | <0.001 |
| LE ECD (Mean ± SD) | 2372.19 ± 190.44 | 2689.76 ± 121.36 | <0.001 |

The coefficient of variation (CV), indicating polymegathism, was significantly higher in the PEX group in both eyes (p < 0.001). Similarly, the percentage of hexagonal cells, reflecting endothelial pleomorphism, was significantly reduced in PEX eyes compared with controls (p < 0.001).

**Comparison of Coefficient of Variation (CV) as an Indicator of Polymegathism Between PEX and Control Eyes.**

| Parameter | PEX Eyes | Control Eyes | p-value |
|---|---|---|---|
| RE CV (Mean ± SD) | 42.87 ± 4.51 | 36.14 ± 2.87 | <0.001 |
| LE CV (Mean ± SD) | 43.21 ± 5.03 | 36.32 ± 2.95 | <0.001 |

Central corneal thickness (CCT) was significantly lower in the PEX group than in controls, with mean values of 519.84 ± 28.62 µm versus 532.17 ± 22.54 µm in the right eye (p = 0.006) and 518.77 ± 29.41 µm versus 531.46 ± 23.08 µm in the left eye (p = 0.005).

**Comparison of Central Corneal Thickness (µm) Between PEX and Control Eyes**

| Parameter | PEX Eyes | Control Eyes | p-value |
|---|---|---|---|
| RE CCT (Mean ± SD) | 519.84 ± 28.62 | 532.17 ± 22.54 | 0.006 |
| LE CCT (Mean ± SD) | 518.77 ± 29.41 | 531.46 ± 23.08 | 0.005 |

Correlation analysis demonstrated a weak negative association between age and endothelial cell density in the PEX group; however, the relationship was not statistically significant (right eye: r = −0.116, p = 0.412; left eye: r = −0.109, p = 0.436).

**Correlation Between Age and Endothelial Cell Density in the PEX Group**

| Variable | Correlation Coefficient (r) | p-value |
|---|---|---|
| Age vs RE ECD | -0.116 | 0.412 |
| Age vs LE ECD | -0.109 | 0.436 |

When mean values of both eyes were analyzed, patients with PEX exhibited a significant reduction in ECD (mean difference: −328.72 cells/mm²; 95% CI: −370.93 to −286.52; p < 0.001), increased CV (+6.81; 95% CI: 5.62–8.00; p < 0.001), reduced hexagonality (−9.76%; 95% CI: −11.02 to −8.50; p < 0.001), and decreased CCT (−12.51 µm; 95% CI: −21.08 to −3.94; p = 0.004).

**Mean difference of endothelial parameters between PEX group and Control Group.**

| Parameter | Mean Difference | 95% CI | p-value |
|---|---|---|---|
| ECD | -328.72 | -370.93 to -286.52 | <0.001 |
| CV | +6.81 | 5.62 to 8.00 | <0.001 |
| HEX | -9.76 | -11.02 to -8.50 | <0.001 |
| CCT | -12.51 | -21.08 to -3.94 | 0.004 |

Overall, pseudoexfoliation syndrome was associated with significant quantitative and morphological alterations of the corneal endothelium, characterized by reduced endothelial cell density, increased polymegathism, increased pleomorphism, and reduced central corneal thickness.

**Discussion**

The present study demonstrated significant corneal endothelial alterations in patients with pseudoexfoliation (PEX) syndrome compared with age-matched controls. PEX eyes showed significantly reduced endothelial cell density (ECD), increased coefficient of variation (CV), decreased hexagonality (HEX), and reduced central corneal thickness (CCT), indicating endothelial cell loss, polymegathism, pleomorphism, and compromised endothelial function.(11,14)

Our findings are consistent with previous studies reporting significant endothelial cell loss and morphological abnormalities in PEX syndrome. Aoki et al. demonstrated that PEX is an independent risk factor for endothelial cell loss, while Nagle and Kulkarni reported significantly reduced ECD, increased CV, reduced hexagonality, and thinner corneas in PEX eyes compared with controls. Similar observations were reported by Iqbal et al. and Songur et al., confirming that deposition of pseudoexfoliative material adversely affects corneal endothelial morphology and function.(11,14)

The absence of significant differences in intraocular pressure and the lack of correlation between age and endothelial cell density in the present study suggest that endothelial damage is primarily related to the pseudoexfoliative process rather than aging alone or elevated intraocular pressure. Previous studies have similarly reported that endothelial alterations may occur even in PEX patients without glaucoma, indicating direct involvement of pseudoexfoliative material in endothelial degeneration.(11,13)

Overall, the present findings confirm that pseudoexfoliation syndrome causes significant structural and morphological compromise of the corneal endothelium. Non-contact specular microscopy is a reliable, non-invasive technique for early detection of these endothelial changes and provides valuable information for preoperative evaluation and surgical planning, particularly before cataract surgery in patients with PEX.(12,15)

**Summary**

This study assessed corneal endothelial changes in patients with pseudoexfoliation (PEX) syndrome using non-contact specular microscopy and compared them with age-matched healthy controls. A total of 104 participants (208 eyes) were included, with 52 PEX patients and 52 controls.

PEX eyes showed significantly lower endothelial cell density, higher coefficient of variation, reduced hexagonality, and thinner central corneal thickness, indicating endothelial loss and morphological damage. These changes were observed even without elevated intraocular pressure, suggesting they are part of the disease process itself.

The findings support routine corneal endothelial evaluation in PEX patients. Non-contact specular microscopy is a safe and useful tool for detecting endothelial abnormalities and identifying patients at risk of corneal complications, especially before intraocular surgery.

**Conclusion**

Study demonstrates that pseudoexfoliation syndrome is associated with significant corneal endothelial alterations, including reduced endothelial cell density, increased coefficient of variation, decreased hexagonality, and reduced central corneal thickness compared with age-matched controls. These findings indicate endothelial cell loss and morphological instability in PEX eyes.The endothelial changes observed appear to be disease-related rather than age-dependent and may occur even in the absence of elevated intraocular pressure. Non-contact specular microscopy proved to be a safe, reliable, and effective method for detecting these alterations.

Routine preoperative endothelial assessment in patients with pseudoexfoliation syndrome is recommended, particularly before intraocular surgery, to identify high-risk eyes, optimize surgical planning, and reduce postoperative corneal complications.

**Strengths**

- Use of non-contact specular microscopy, a safe, non-invasive, and reliable method for assessing corneal endothelial parameters
- Inclusion of an age-matched control group, ensuring valid comparison and minimizing age-related bias
- Evaluation of multiple endothelial parameters (ECD, CV, HEX, CCT) providing a comprehensive assessment
- Standardized methodology with same examiner and repeated measurements, reducing inter-observer variability
- Clear inclusion and exclusion criteria, improving internal validity of the study

**Limitations**

- Cross-sectional study design, limiting the ability to assess progression of endothelial changes over time
- Relatively small sample size, which may affect the generalizability of results
- Conducted at a single tertiary care center, limiting external validity
- Lack of subgroup analysis based on disease duration or severity (e.g., PEX vs PXG)
- Potential influence of unmeasured confounding factors such as environmental or genetic variables

**Conflict of interest:** There is no conflict of interest.
**Ethical statement:** Informed consent was obtained from the patient prior to all clinical investigations and procedures. All efforts have been made to ensure patient anonymity and confidentiality.

**Financial support and sponsorship:** Nil

**Author contribution:**
**Sonia:** Conceptualization, patient recruitment, data collection, clinical examination, manuscript preparation and literature review**.**
**Suman Chahar:** Study supervision, methodology development, data interpretation, manuscript review, and academic guidance throughout the study.
**Vandana Mahur:** Study conception, overall supervision, validation of methodology, critical review of the manuscript, administrative support, and final approval of the manuscript.
**T.S. Ahluwalia**: Study conception, overall supervision, validation of methodology, critical review of the manuscript, administrative support, and final approval of the manuscript.

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