

# Evaluation of Morphological Changes in Corneal Endothelial Cells and Central Corneal Thickness in Pseudoexfoliation Syndrome

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## Abstract

**Background:** Pseudoexfoliation causes characteristic corneal endothelial changes leading to corneal decompensation and loss of corneal transparency severely affecting vision. **Objectives:** To evaluate morphological changes in corneal endothelial cells and central corneal thickness in pseudoexfoliation syndrome (PXS) and to compare it with age matched patients without pseudoexfoliation syndrome. **Material and Methods:** A hospital based, cross sectional analytical study was conducted at Upgraded Department of Ophthalmology, Government Medical College/hospital, Jammu in which total of 46 patients planned for cataract surgery were included (23 patients with pseudoexfoliation syndrome and 23 patients without pseudoexfoliation syndrome). Corneal endothelial cell density (ECD), percentage of hexagonal cells, coefficient of variation (CV) in cell size, and central corneal thickness (CCT) were measured using specular microscopy. **Results:** The mean ECD was  $2325.1 \pm 383.1$  in the PXS group and  $2763 \pm 351.3$  in the control group respectively, and ECD in the PXS group was significantly lower than that in the control group ( $p=0.0002$ ). The percentage of hexagonal cells was  $48.3 \pm 5.7$  in PXS group and  $51.5 \pm 4.6$  in the control group respectively, and percentage of hexagonal cells was significantly lower than that in the control group ( $p=0.04$ ). The cell size coefficient of variation was  $33.9 \pm 2.6$  in the PXS group and  $33.0 \pm 3.1$  in the control group respectively, and patients with PXS had no statistically significant difference in cell size coefficient of variation compared to control group ( $p=0.29$ ). The CCT was  $509.0 \pm 27.3$  in the PXS group and  $529.0 \pm 23.6$  in the control group respectively, and CCT in the PXS group was significantly lower than that in the control group ( $p=0.01$ ). **Conclusion:** In our study the ECD and CCT was significantly lower in patients with pseudoexfoliation syndrome regardless of the presence of pseudoexfoliative glaucoma.

## Keywords

Corneal endothelium, Central corneal thickness, Pseudoexfoliation syndrome, Specular microscopy.

## Introduction

The pseudoexfoliation syndrome (PXS) is an age-related systemic disorder with a strong genetic predilection.<sup>[1,2]</sup> It is characterized by the formation and gradual deposition of extracellular granular material on various intraocular

structures.<sup>[3]</sup> In the eye PXS syndrome is characterized by white deposits seen on the pupillary border and anterior lens capsule, iris epithelium, inner layer of ciliary epithelium, anterior chamber angle structures, on the

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zonules of zinn, and front part of vitreous. [4] The material has also been reported along vascular endothelium, corneal epithelial basement membrane and corneal stroma. [4] Pseudoexfoliative material deposition involving anterior segment of the eye can lead to cataract, secondary open angle glaucoma, blood aqueous barrier dysfunction, lens subluxation, retinal vein occlusion and corneal endothelial decompensation. [2,5,6]

Corneal transparency depends upon functional and morphological integrity of corneal endothelium. [7] Pseudoexfoliation causes increased oxidative stress to the corneal stroma which causes a decline in the number of keratocytes ultimately leading to the damage of its extracellular structure which may result in reduced central corneal thickness. [8,9] The progressive loss of endothelium due to chronic disorders affects the functioning and transparency of cornea. If the ECD is less than 500/mm<sup>2</sup> corneal decompensation occurs causing corneal oedema and bullous keratopathy. [10] The aim of this study was to evaluate corneal endothelial changes and central corneal thickness in patients with pseudoexfoliation syndrome and compare it with age matched controls without pseudoexfoliation syndrome.

### Material and Methods

A hospital based cross-sectional analytical study was conducted at Upgraded Department of Ophthalmology, Government Medical College/Hospital, Jammu in which 23 patients with age of 50 years or older of either sex with pseudoexfoliation syndrome and 23 age matched controls without pseudoexfoliation syndrome planned for cataract surgery were evaluated after approval of the Institutional Ethics Committee. Exclusion criteria included patients with any previous history of ocular surgery or ocular trauma, any ocular inflammatory disease, history of diabetes, glaucoma, previous laser treatment and contact lens users.

All patients underwent a thorough ophthalmic examination including visual acuity both distant using Snellen's chart and near using Jaeger's chart, IOP measurement using non-contact tonometry, slit-lamp examination of anterior segment and fundoscopy was done after written informed consent. Diagnosis of PXS was made on the basis of typical slit lamp appearance of pseudoexfoliative material at the anterior lens capsule and/or at the pupillary margin. The corneal endothelial morphology was evaluated using TOPCON Specular microscope (Fig. 1). The parameters included endothelial cell density, co-efficient of variation

and percentage of hexagonal cells. The central corneal thickness was also evaluated using specular microscopy.



**Figure 1: Specular Photomicrography from Topcon**

Statistical analysis was done by using SPSS software version 25. Data was depicted as mean  $\pm$  standard deviation (SD). Comparison of quantitative data was done by unpaired sample *t*-test and value of  $p < 0.05$  was considered statistically significant and qualitative data by chi-square test.

### Results

The study included 46 patients planned for cataract surgery, who were divided into two groups: 23 patients (Males-13 and Females- 10; Age range 59-92) with pseudoexfoliation syndrome and 23 age matched patients (Males- 15 and Females- 8; Age range 55-90) without pseudoexfoliation syndrome ( $p=0.8$ ). The demographic characteristics of both the groups are summarized in *Table 1*.

The corneal endothelial characteristics and CCT of the both the groups are summarized in *Table 2*. The patients with PXS had statistically significant decreased mean value of ECD ( $2325.1 \pm 383.1$  vs CNT  $2763 \pm 351.3$ ) ( $p=0.0002$ ) with lower percentage of hexagonal cells ( $48.3 \pm 5.7$  vs CNT  $51.5 \pm 4.6$ ) ( $p=0.04$ ) and statistically significant decreased mean value of CCT ( $509.0 \pm 27.3$  vs CNT  $529 \pm 23.6$ ) ( $p=0.01$ ). Patients with PXS had no statistically significant difference in cell size coefficient of variation ( $33.9 \pm 2.6$  vs CNT  $33.0 \pm 3.1$ ) ( $p=0.29$ ).

ECD value of 2000 cells/mm<sup>2</sup> is taken as reference limit for the risk of corneal decompensation and values less than 2000 are considered high risk. In our study 26% patients in PXS group had values  $<2000$  vs CNT in which only 4.4% patients had risk of corneal decompensation as shown in *Table 3*.

**Table 1: Demographic Characteristics**

Groups	PXS	CNT	<i>p</i> value
Number of Patients	23	23	
Gender	M- 13 (56.5%) F- 10 (43.5%)	M- 15 (65.2%) F- 8 (34.8%)	0.76 (>0.05)
Age (Mean ± SD)	69.1 ± 10.6	70.0 ± 11.4	0.8 (>0.05)
Range	59-92	55-90	

PXS: Pseudoexfoliation syndrome; CNT: Control group; M: Male; F: Female

**Table 2: Corneal Endothelial Characteristics and CCT of Both the Group**

Characteristics	PXS (Mean ± SD)	CNT (Mean ± SD)	<i>p</i> value
ECD (cells/mm <sup>2</sup> )	2325.1 ± 383.1	2763 ± 351.3	0.0002
Cell size variation coefficient (%)	33.9 ± 2.6	33.0 ± 3.1	0.29
Hexagonality (%)	48.3 ± 5.7	51.5 ± 4.6	0.04
CCT (µm)	509 ± 27.3	529 ± 23.6	0.01

ECD: Endothelial cell density; CCT: Central corneal thickness.

**Table 3: The Risk of Corneal Endothelial Decompensation**

Groups	ECD<2000 cells/mm <sup>2</sup>	ECD 2000 cells/mm <sup>2</sup>
PXS	26.0%	74.0%
CNT	4.4%	95.6%

## Discussion

Pseudoexfoliation syndrome significantly causes reduction in corneal endothelial cell density. The reduced ECD in PXS is due to the deposition of pseudoexfoliating material on the corneal endothelium which penetrates towards Descemet's membrane causing breakdown of connections between individual hexagonal cells resulting in apoptosis of these cells. Various other factors in addition to deposition of pseudoexfoliating material leading to reduced ECD include hypoxia of anterior chamber, elevated concentration of TGF α1 and changes in fibroblasts of the endothelium. [11] The apoptosis of corneal stromal keratocytes leads to depletion of its extracellular structure. This may result in reduced CCT

and more susceptibility to raised intraocular pressure.

Our study analysed corneal endothelial cell characteristics and central corneal thickness in pseudoexfoliation syndrome. Statistical calculations demonstrated that mean ECD 2325.1 ± 383.1 in the PXS group was lower than in the control group 2763 ± 351.3 with statistical significance (*p*=0.0002). The results of our study are consistent with the studies by Zheng et al., [8] Kovalionas et al. [12] and Zarnowski et al. [13] All these studies reported statistically significant lower ECD in PEX group compared to controls. Our study did not include patients with any history of ocular surgery/ trauma suggesting that pseudoexfoliation may cause corneal endothelial cell loss.

ECD value of 2000 cells/mm<sup>2</sup> is taken as reference limit to assess the risk of corneal decompensation and values less than 2000 are considered high risk. 26% patients in our study group had elevated risk of corneal decompensation. The results are consistent with the study by Quiroga et al. [14] which demonstrated that 21.3% patients had ECD less than 2000. All the points highlighted above should be considered during preparation of patients with PXS undergoing intraocular surgery as it has been suggested by previous studies that ECD loss of about

9% occurs three months post cataract surgery.<sup>[15]</sup> Our study demonstrated more polymegathism in PXS group with no statistical significance ( $p=0.29$ ) which is consistent with the study by Inoue et al.<sup>[16]</sup> In our study pleomorphism was also more in PXS group compared to controls with statistical significance ( $p=0.04$ ) which is similar to results demonstrated by Sarowa et al.<sup>[17]</sup> In our study the mean CCT  $509.0 \pm 27.3$  in PXS group was lower than in the control group  $529.0 \pm 23.6$  with statistical significance ( $p=0.01$ ). The result of our study is consistent with the study by Spoorthy et al.<sup>[18]</sup> in which they found PEX group had thinner cornea ( $p<0.05$ ). The results of our study were also similar to the study conducted by Asritha et al.<sup>[19]</sup> Results obtained by Hepsen et al.<sup>[20]</sup> (PEX= $546.6 \pm 39.6$  versus NO PES= $542.9 \pm 32.2$ ) and Arnarsson et al.<sup>[21]</sup> (PEX= $533 \pm 32$  versus NO PEX= $527 \pm 40$ ) with no statistical significance were inconsistent with our study.

### Conclusion

In our study the ECD and CCT were significantly lower in patients with pseudoexfoliation syndrome regardless of the presence of pseudoexfoliative glaucoma which may increase the risk of corneal decompensation after intraocular surgeries. Therefore, a proper pre-operative evaluation must be done in all the patients with pseudoexfoliation syndrome undergoing intraocular surgeries.

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### Conflicts of Interest

There are no conflicts of interest.

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