

## COMPARISON OF CORNEAL ENDOTHELIAL CELL DENSITY IN PATIENTS OF PSEUDOEXFOLIATION SYNDROME WITH NORMAL POPULATION

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### ABSTRACT

**Objective:** To compare the corneal endothelial cell density in patients of Pseudoexfoliation syndrome (PXS) with normal healthy controls.

**Study Design:** Cross sectional comparative.

**Place and Duration of Study:** This study was carried out at Armed Forces Institute of Ophthalmology, Rawalpindi from Mar 2016 to Jan 2017.

**Patients and Methods:** Patients of PXS and healthy subjects of both genders between ages of 40 and 50 years, with best corrected visual acuity of 6/6 on snellen visual acuity chart were included in the study. All the participants including controls and PXS patients were subjected to ophthalmic clinical examination including corrected distance visual acuity, slit lamp examination by the single trainee researcher to exclude bias. Participants in both groups were evaluated for corneal endothelial cell density (ECD) by using non-contact, TOPCON SP 3000P Specular microscope. Sampling bias was eliminated by analyzing 100 cells in the center of each specular microscope photograph and mean of three readings was analyzed.

**Results:** Both the groups were similar with respect to gender and age. In our study sample there were 29 (58%) males in PXS group and 24 (48%) males in control group with no statistical significant ( $p$ -value  $> 0.05$ ) difference between gender distributions of both groups. The mean age of the PXS group was  $46.34 \pm 2.932$  years, and in control group was  $45.54 \pm 2.887$  years ( $p$ -value  $> 0.05$ ). The mean value of ECD was found to be  $2021.548 \pm 528.142$  cells/mm<sup>2</sup> in PXS patients and the mean value of ECD in healthy subjects was noted to be  $2772.692 \pm 383.395$  cells/mm<sup>2</sup>, showing significantly lower ECD in PXS cases. Similarly, significantly higher number of cases 22 (44%) had CED  $< 2000$  in PXS as compared to normal healthy subjects.

**Conclusion:** Corneal endothelial cell density decreases in patients of pseudoexfoliation syndrome and this must be considered while planning any intraocular surgery including cataract extraction.

**Keywords:** Corneal endothelial cell density, Intraocular surgery, Pseudoexfoliation syndrome.

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### INTRODUCTION

Cornea is the most important refractive surface of human eye, with maximum contribution towards refraction of light. Corneal pathology comprises a vast spectrum of diseases which may affect its transparency. Structural damage, particularly during intraocular surgery can affect its clarity eventually resulting in reduced vision and poor quality of life<sup>1</sup>.

Cornea is a multilayered structure with each layer performing specific function. The innermost

layer of cornea is the endothelium, a monolayer of polygonal cells. The cells are peculiar in a way that they cannot regenerate, and any damage results in permanent loss of endothelium. The normal corneal endothelial-cell density (ECD) is about 2600 cells/mm<sup>2</sup>. There is an estimate that the number of cells decreases at about 0.6% per year. Endothelial damage can be due to inadvertent endothelial trauma from cataract surgery, malpositioned intraocular lens or infections<sup>2</sup>. The endothelial cell count is also affected by age related changes which make it more susceptible to oxidative damage<sup>3-5</sup>. Pseudoexfoliation syndrome is a condition afflicting the cornea that can affect various ocular

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measurements such as central corneal thickness and intraocular pressure<sup>6</sup>.

There is a greater variation in prevalence rate of Pseudoexfoliation syndrome in different geographical locations. Its prevalence in Asian countries is quite high with Iran having a prevalence of 9.6%<sup>7</sup>. It is similar in India (3.8%)<sup>8</sup> and Japan (3.4%)<sup>9</sup>. The prevalence of PXS is very truncated in Singapore (0.32%)<sup>10</sup> and China (0.4%)<sup>11</sup>.

Pseudoexfoliation syndrome (PXS) has significant relation to age. It is a genetically determined condition with deposition of anomalous fibrillary extracellular material on intraocular structures. The material gets deposited on most of the anterior segment structures, including, cornea, iris, ciliary body, lens capsule, zonules and angle. People with PXS are susceptible to open angle glaucoma and complications during cataract surgery including post-operative corneal edema, intraocular pressure elevation, lens subluxation, zonular dehiscence, poorly dilating pupil and posterior capsular rupture. Pre-operative assessment of ECD is an important parameter determining post-operative corneal edema in patients with PXS undergoing cataract surgery<sup>12</sup>.

In vivo microscopy cornea provides high resolution images of the corneal endothelium. Multiple studies have evaluated the differences in ECD between normal population and patients with PXS but no study is available showing the comparison of ECD between normal individuals and patients of PXS in Pakistani population. The evaluation of corneal ECD in patients with PXS will help in predicting patients with high probability for development of corneal edema after cataract surgery in order to warrant effective per op methods to prevent corneal endothelial damage.

## MATERIAL AND METHODS

This was a cross sectional comparative study carried out at Armed Forces Institute of Ophthalmology, Rawalpindi Pakistan from March 2016 to January 2017. The study was

started after taking approval from institutional ethics committee. All the patients were informed about the study and informed written consent was taken from each patient prior to inclusion in the study. Sample size was calculated by WHO sample size calculator using mean ECD in control (normal) group 2570 and in patients with PXS was  $2124 \pm 346$  cells/mm<sup>2</sup>, taking 95% confidence interval and 80% power the test. The sample size was found to be 50 eyes in each group, and a total of 100 eyes were included in the study.

Healthy subjects of both genders between age of 40 and 50 years that have no specific symptoms and patients with PXS between 40 and 50 years of age with best corrected visual acuity of 6/6 on snellen visual acuity chart were included in the study. Patients on any topical medication, connective tissue disease, stromal and endothelial disease, and patients with family history of glaucoma, keratoconus and corneal dystrophy were excluded from the study.

All the participants including Controls and PXS patients were subjected to ophthalmic clinical examination including corrected distance visual acuity and slit lamp examination by the single trainee researcher to exclude bias. Participants in both groups were evaluated for corneal endothelial cell density by using non-contact, TOPCON SP 3000P Specular microscope. Sampling bias was eliminated by analyzing 100 cells in the center of each specular microscope photograph and mean of three readings was used for analysis.

Data was evaluated and analyzed using Statistical program for social sciences (SPSS) version 17. Mean and standard deviation was noted for quantitative variables while frequency and percentage for qualitative data was noted. Normal population and patients with PXS were compared for ECD by independent sample t-test. A *p*-value <0.05 was considered significant.

## RESULTS

In this cross sectional study a total of 100 eyes were included consisting of 50 eyes of normal healthy controls and 50 eyes of patients of

PXS. These groups were similar with respect to gender and age. In our study sample, there were 29 (58%) male and 21 (42%) female in PXS group and in control group there were 24 (48%) males and 26 (52%) females with no statistical significant ( $p$ -value>0.05) difference between gender distribution of both groups. The mean age of the PXS group was  $46.34 \pm 2.932$  years with a range of 40 to 50 years and the mean age in control group was  $45.54 \pm 2.887$  years, ranging from 40 to 50 years with no statistically significant ( $p$ -value>0.05) difference between

both groups showing that the patients with PXS had significantly lower ECD in comparison to healthy controls. The comparison of proportion of ECD <2000 cells/mm<sup>2</sup> and ECD >2000 cells/mm<sup>2</sup> revealed that PXS cases had significantly higher number of cases 22 (44%) having ECD <2000 as compared to normal healthy subject in which only 2 (4%) subject had ECD <2000 cells/mm<sup>2</sup> as given in table-II.

## DISCUSSION

Pseudoexfoliation syndrome is a systemic

**Table-I: Demographic characteristics of participants.**

Characteristics	PXS Cases	Normal Controls	$p$ -value
<b>Gender of the Participant</b>			
Male	29 (58%)	24 (48%)	0.316
Female	21 (42%)	26 (52%)	
<b>Age of the Participant</b>			
Mean $\pm$ SD	$46.34 \pm 2.932$	$45.54 \pm 2.887$	0.172
<b>Categorized Age of the Participant</b>			
40-43	11 (22%)	14 (28%)	0.758
44-46	14 (28%)	14 (28%)	
47-50	25 (50%)	22 (44%)	

**Table-II: Comparison of CED between cases and controls.**

Characteristics	PXS Cases	Normal Controls	$p$ -value
<b>Corneal Endothelial Cell Density</b>			
Mean $\pm$ SD	$2021.548 \pm 528.142$	$2772.692 \pm 383.395$	<0.001
<b>Categorized Corneal Endothelial cell density</b>			
<2000 cells/mm <sup>2</sup>	22 (44%)	2 (4%)	<0.001
>2000 cells/mm <sup>2</sup>	28 (56%)	48 (96%)	

mean ages and age intervals of both groups as elaborated in table-I.

No abnormality was found in cornea on slit lamp biomicroscopy, the only finding on the slit lamp biomicroscopy was pseudoexfoliation in PXS group patients. Table-II shows the summary of comparison of both cases of PXS and control healthy subjects on the basis of quantitative in vivo corneal confocal microscopy findings of the cell density measurements. The mean value of Corneal Endothelial Cell Density (ECD) was  $2021.548 \pm 528.142$  cells/mm<sup>2</sup> in PXS patients and the mean value of ECD in healthy subjects was  $2772.692 \pm 383.395$  cells/mm<sup>2</sup> with statistically significant ( $p$ -value <0.05) difference between

disease which is detectable in eyes. Pseudoexfoliative material gets deposited on various anterior segment structures. The nature of this material is mostly fibrillar which is coated with amorphous material. These fibrils are composed of different component of cellular membranes and enzymes involved in extracellular matrix maintenance. PXS is considered as important cause of secondary open-angle glaucoma called pseudoexfoliation glaucoma (PXG) globally<sup>13</sup>.

Human cornea is a delicate structure which consists of 5 layers with endothelium, which is only one cell thick being the most important. Any damage to endothelial cell layer results in permanent cell loss and ultimately requiring

corneal transplant when it reduces to a certain low count. With aging all the corneal layers become susceptible to oxidative damage<sup>14</sup>.

It has been noted in previous researches that age is an independent factor, which cannot be considered for alteration of corneal ECD while planning any intraocular surgery. Pseudoexfoliation syndrome (PEX) is thought to be a basement membrane disease in which ocular signs are easily recognized by deposition of dandruff like material on various ocular structures including cornea, pupillary margin and lens<sup>15</sup>.

In our study, we studied the endothelial cell density and tried to find out whether there is an impact of PXS on ECD. There is discrepancy in the literature about the effect of PXS on ECD in different populations like Indian, Filipino, Iranian, Thai, Chinese, Japanese, and American populations. A very small number of studies in literature have actually studied corneal ECD in patients of pseudoexfoliation in our population. In this present study, patients of PXS and control healthy subjects were compared on the basis of quantitative in vivo corneal confocal microscopy findings of the cell density measurements. The mean value of Corneal Endothelial Cell Density was  $2021.548 \pm 528.142$  cells/mm<sup>2</sup> in PXS patients in comparison to  $2772.692 \pm 383.395$  cells/mm<sup>2</sup> in healthy subjects with significant ( $p$ -value<0.05) difference between both groups showing the patients with PXS had significantly lower ECD in comparison to healthy controls.

Like us, several authors have come up with similar results in their respective studies. Oltulu et al in their study on 57 patients concluded that mean ECD in control (normal) group was  $2570 \pm 369$  cells/mm<sup>2</sup> while in patients with PXS was  $2124 \pm 346$  cells/mm<sup>2</sup>. The difference between both groups was statistically significant ( $p$ <0.001)<sup>12</sup>. Zheng et al in his study on 27 patients with unilateral PXS and 27 normal controls showed mean ECD in control group to be  $2738.7 \pm 233.2.6$  cells/mm<sup>2</sup> and PXS group to  $2240.7 \pm 236.6$  cells/mm<sup>2</sup><sup>16</sup>.

Various studies have described the changes in the histopathological endothelial characteristics, although few used in vivo corneal confocal microscopy to analyze the possible differences between patients with and without PEX<sup>17,18</sup>. Zheng et al. observed not only lower endothelial cell density but also increased degrees of pleomorphism and polymegathism and a higher coefficient of variation in the cell sizes in the patients with PEX compared with those in the healthy control subjects<sup>16</sup>.

The PXS causes changes in corneal endothelium in patients of PXS which might be problematic when these patients require intraocular surgery. Many studies have reported that PXS elevated the risk of corneal endothelial decay, when these PXS patients undergo cataract surgery. In a study by Quiroga it was noted that 21.87% patients of PXS had endothelial cell density less than 2000 cells/mm<sup>2</sup>, which might be very risky<sup>19</sup>. In our study the comparison of proportion of ECD <2000 cells/mm<sup>2</sup> and ECD >2000 cells/mm<sup>2</sup> revealed that PXS cases had significantly higher number of cases 22 (44%) having ECD <2000 as compared to normal healthy subject in which only 2 (4%) subject had ECD <2000 cells/mm<sup>2</sup>. Therefore, it is recommended that PXS patients should be evaluated for corneal endothelium cell density before planning the intraocular surgery.

The results of our study clearly revealed that pseudoexfoliation syndrome is a common condition taking its toll on the corneal ECD. We consider our findings, significant for Pakistani population and hence worth reporting. However, we do recommend that studies with longer duration and considering confounding variables should be done to yield more comprehensive results.

## CONCLUSION

Our study reveals that eyes with PXS have lower cell densities as compared to control subjects. It is concluded that corneal endothelial cell density decreases in patients of pseudoexfoliation syndrome and this must be

considered while planning any intraocular surgery on these eyes including cataract extraction.

### CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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