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Age Matched Corneal Endothelial Cell Count in Patients with Pseudo Exfoliation Syndrome

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ABSTRACT

Objective: To evaluate corneal endothelial cell count (CECC) in patients with Pseudo Exfoliation Syndrome (PEX) and control participants of matched age along with comparing intra ocular pressure (IOP) between the two groups.
Study Design: Comparative Cross Sectional Study.
Place and Duration of Study: Armed Forces Institute of Ophthalmology Rawalpindi, Pakistan from Dec 2022 to May 2023.
Methodology: A total of 70 participants were enrolled for this cross-sectional analysis through two matched sample groups which included 35 individuals with Pseudo exfoliation syndrome (PEX) and 35 control subjects without Pseudo exfoliation syndrome. A statistical evaluation compared corneal endothelial cell count using specular microscopy and IOP measurement (by Goldman applanation tonometry) between study groups.
Results: The PEX group demonstrated reduced mean Corneal endothelial cell count (CECC) measurements at 1768.29±213.53 cells/mm² compared to control group CECC (2245.89±187.70cells/mm²) with $p<0.001$ statistical significance. The mean IOP of PEX group was19.90±2.40 mmHg and control group was 15.10±1.80 mmHg. The p-value<0.001 of IOP shows that a direct link between PEX and higher IOP The PEX group showed a negative moderate correlation between CECC and patient age (r = -0.57 p=0.747) which demonstrates CECC decreases in advanced age. The IOP and CECC had strong positive correlation (r = 0.966, p<0.001).
Conclusions: Patients with pseudo exfoliation syndrome showed reduced corneal endothelial cell count (CECC) and higher IOP measurements as compared to the age matched control group.

Keywords: Corneal endothelial cell count, Glaucoma, Intraocular pressure, Pseudo exfoliation syndrome, Intraocular pressure, Specular microscopy.

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INTRODUCTION

Pseudo exfoliation syndrome (PEX) functions as a multi organ disorder which also targets the intra-ocular tissue by producing extracellular abnormal whitish fibrillar material.[1] The prevalence of PEX tend to increase with age.[2] Intra-ocular structures that have shown accumulation of pseudo exfoliative material include cornea, iris, lenticular zonules and trabecular meshwork. Open-angle glaucoma may develop secondary to PEX deposition in trabecular meshwork while the condition also serves as a risk factor for cataract with zonular weakness.[3] The corneal endothelium is a mono-layered hexagonal cellular membrane that does not have the ability to regenerate. The normal density of corneal endothelial cells in adults is approximately 2763.6 cells/mm² on average.[4] Corneal transparency being of prime importance ensuring visual clarity depends mainly on the corneal endothelial condition. The syndrome is thought to affect both density and quality of corneal endothelial cells.[5] As a result, decreased corneal endothelial cell count leads to imbalanced corneal hydration state which has worsening effects on vision.[6] Scarcely understood pseudo exfoliation syndrome pathophysiology might relate to both genetic and environmental elements. The syndrome influences both anterior and posterior segments however corneal endothelial cell density reduction stands as the main aspect of interest in this study.[7] Literature shows age as another important factor as the corneal endothelial cell count decreases throughout life.[8] This study points to the patients with PEX have their corneal endothelial cell count decrease more quickly than others thus promoting concerns for lasting corneal health and possible complications related to corneal endothelial dysfunction.[9]

This study aimed to evaluate corneal endothelial cell count (CECC) between PEX patients and control participants of matched age along with a comparison of intra-ocular pressure between the two groups.

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METHODOLOGY

A comparative cross-sectional study was conducted at Armed Forces Institute of Ophthalmology, Rawalpindi, Pakistan. The study was conducted from December 2022 till May 2023. It evaluated the corneal endothelial cell count (CECC) between PEX patients and healthy subjects matched by age. Ethical permission was taken from ethical review board of AFIO and granted ethical permission (287/ERC/AFIO, dated 20 Nov 2022) The sampling technique was non-probability purposive. Sample size was calculated using WHO sample size calculator taking confidence interval 95%, margin of error 5%, The mean of Corneal Endothelial Cell Density in PXS was 2021.548±528.142 and in normal control was 2772.692±383.395.[10] The estimated sample size came out to be 12 patients (06 each group) but we took 70 Patients (35 each group).

Inclusion Criteria: Individuals having PEX only confirmed on slit lamp examination were included in Group-A. whereas Group-B features participants with healthy eyes free of any anterior or posterior segment disease.

Exclusion Criteria: Individuals with known corneal diseases, cataract, previous ophthalmological procedures including cataract surgery and posterior segment diseases were not included in the study. Individuals using any ocular therapeutic drugs in last 3 months were also excluded.

The collected data gathered included demographic information from every participant regarding their age, gender and medical background. All participants underwent a thorough ocular examination which included visual acuity assessment (for far and near) using standard Snellen's chart, IOP measurement using Goldmann applanation tonometry. Detailed slit lamp examination of anterior segment was done to confirm presence of PEX and to rule out pre-existing corneal diseases, cataract and any other anterior segment disease that may affect corneal endothelium health using Slit lamp microscope SM-30N (Takagi, Japan). Assessment of posterior segment including optic disc evaluation using non-contact aspheric Super field 90 D lens (Volk, USA), was performed to rule out any signs of glaucoma or other posterior segment diseases. Corneal endothelial cell count was measured using specular microscope SP-3000P (Topcon, Japan). A total of 3 readings were recorded, and their average was considered. Visual field 30-2 test was carried out using Humphrey Field Analyzer 3 (Zeiss, Germany).

To statistically analyze the collected data, Statistical Package for Social Sciences (SPSS) software version 22 was used. Normality of data was checked by Shapiro-Wilk test that showed all the parameter were normally distributed as *p*-values>0.05. Quantitative variables (age, IOP, CECC (PEX) were presented as Mean±SD. Qualitative variables (gender) were presented as frequency and percentages.

The independent sample t test was used for quantitative variable and chi square was for qualitative variables. Pearson's correlation was relationship between Corneal endothelial cell count (CECC) and Clinical Parameters in PEX Group. A *p*-value ≤0.05 was considered as significant.

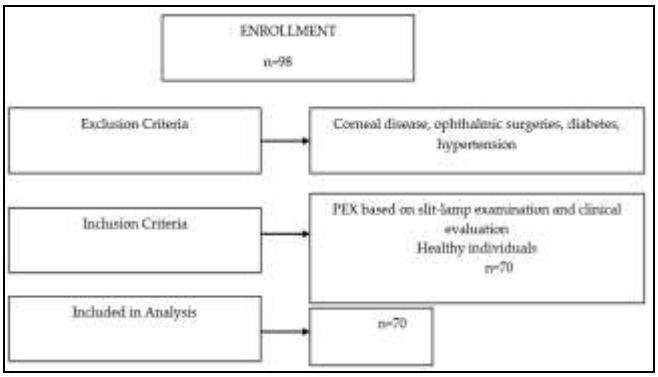

Figure-1: Consort Flowchart Diagram for Participants Selection n=70

RESULTS

A total 70 Patients, (35 patients each group) included in this study. The mean age of PEX group of patients was 67.50±5.20 years and control group was 68.10±5.00 years. However, gender distribution of both groups was similar. There was not statistically significant found in age and gender among the study groups as *p*-values > 0.05. The mean IOP of PEX group was 19.90±2.40 mmHg and control group was 15.10±1.80 mmHg. The *p*-value <0.001 of IOP shows that a direct link between PEX and higher IOP. Additional evidence from this study confirmed the previously documented relationships between PEX with higher IOP as documented in Table-I.

The PEX group contained less corneal endothelial cells than the control group according to the specular microscopy results. Corneal endothelial cell count (CECC) measurements at 1768.29±213.53 cells/mm² compared to control group CECC

(2245.89±187.70cells/mm²). The *p*-value<0.001 indicated a strong statistical difference of CECC among the groups.

Table-I: Demographic and Clinical Characteristics of Participants (n=70)

Characteristic	PEX Group-A (n=35)	Control Group-B (n=35)	*p*-value
Age (years)	67.50±5.20	68.10±5.00	0.65
Gender			
Male Female	18(51.4%) 17(48.6%)	18(51.4%) 17(48.6%)	1.00
Mean Intra Ocular Pressure (mmHg)	19.90±2.40	15.10±1.80	<0.001

The PEX group showed a negative moderate correlation between CECC and patient age (r = -0.57 *p*=0.747) which demonstrates CECC decreases in advanced age. The Intra Ocular Pressure (IOP) and CECC had strong positive correlation (r=0.966, *p*< 0.001) because relative higher IOP leads to higher CECC density as confirmed by current knowledge on corneal endothelial cell responses to high intraocular pressure (Figure-2).

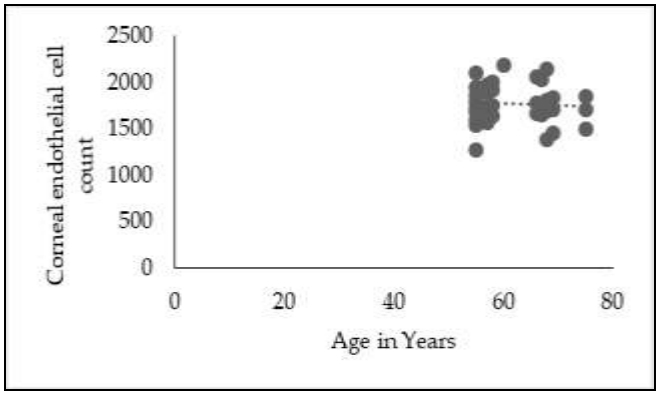

Figure-2a: Relationship of Age and CECC in PEX Group (n=35)

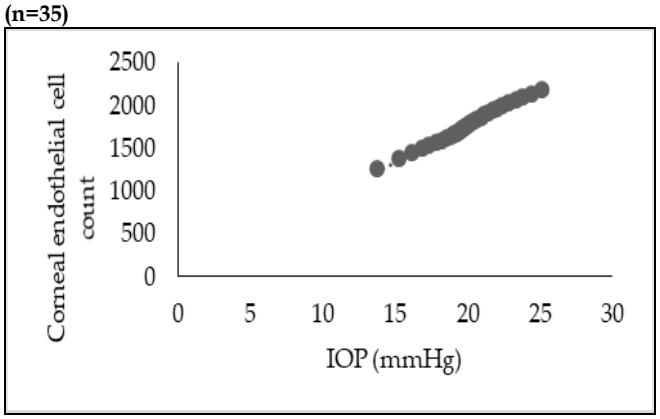

Figure-2b: Relationship of IOP and CECC in PEX Group (n=35)

Figure-2: Relationship of Corneal Endothelial Cell Count (CECC) with Age and Intra Ocular Pressure (IOP) (n=35)

The PEX group presented statistically significant lower Central Endothelial Cell Density compared to controls throughout the examined age ranges. Results revealed that individuals in the age range of 50-59 within the PEX group displayed a mean CECC of 2031.85±195.80cells/mm² which proved considerably lower than the 2175.67±180.25cells/mm² recorded in the control group (*p*=0.001). The PEX patients within the age range of 60-69 exhibited CECC values of 1600.99±210.04cells/mm² which proved statistically lower when compared to the control group measure of 2585.15±170.45 cells/mm² (*p*<0.001). The patient group with PEX demonstrated a CECC measurement of 1320.62±230.54 cells/mm² during the 70-75 age period which produced significant results below the control group CECC measurement of 1970.86±150.83cells/mm² at *p*<0.001. The results show that PEX reduces the CECC scores for patients in each age bracket of the testing population according to Table-III.

Table-II: Corneal Endothelial Cell Count (CECC) Comparison in PEX and Control Groups (n=70)

Parameters	PEX Group-A (n=35)	Control Group-B (n=35)	*p*-value
Mean of CECC (cells/mm²)	1768.29±213.53	2245.89±187.70	<0.001

PEX:Pseudo Exfoliation Syndrome, CECC:Corneal Endothelial Cell Count

Table-III: Comparison of Corneal Endothelial cell Count (CECC) by Age Groups Among Groups

Age Group (years)	PEX Group-A CECC (cells/mm²) n=35	Control Group-B CECC (cells/mm²) n=35	*p*-value
50-59	2031.85±195.80	2175.67±180.25	0.001
60-69	1600.99±210.04	2585.15±170.45	<0.001
70-75	1320.62±230.54	1970.86±150.83	<0.001

Note: Data are presented as mean ± SD. p-values calculated using independent t-test for each age group comparison. PEX:Pseudo Exfoliation Syndrome, CECC: Corneal endothelial cell count

DISCUSSION

This study evaluated the corneal endothelial cell count (CECC) in patients with pseudo exfoliation syndrome (PEX) while measuring it against an age-fitted control group. The PEX group presented with statistically reduced CECC compared to the control group thus confirming past studies that link pseudo exfoliation syndrome to corneal endothelial cell depletion.[11,12] The PEX patients demonstrated a mean corneal endothelial cell count of 1705±212 cells/mm² which represented a significant difference compared to the control subjects who showed 2284±182

cells/mm² (p<0.001). Similar research has established that PEX patients exhibit endothelial cell loss because of elevated IOP and normal age-related deterioration.[13] Research conducted by Tekce *et al.*, (2020) confirmed PEX patients displayed prominently reduced CECC values than healthy control participants from the same age group.[14] The pseudo exfoliation disease diminishes cell density to levels comparable with the findings in this study thus demonstrating its damaging effects on endothelial tissue especially when combined with elevated IOP or other age-related variables. The investigation by Javagal *et al.*, (2023) also showed PEX patients had reduced CECC levels because they presented higher glaucoma risks which frequently develop in patients with PEX.[15]

The current study analyzed the relationship between CECC measurements and clinical scoring factors which included patient age together with Intraocular Pressure readings. The present findings indicate that age demonstrates a moderate negative influence on CECC levels similarly to Ucar *et al.*, (2021) who found aging as a key cause of endothelial cell depletion affecting more the PEX patients than normal subjects.[16] The high IOP combined with impaired endothelial cell regenerative abilities explains why these patients show signs of damage.[17,18]

LIMITATION OF STUDY

Our research does not investigate relation of PEX with chances of glaucoma development and other complications. long-term corneal endothelial functions or how endothelial cells may be safeguarded from adverse effects of PEX syndrome. Future research should include bigger participant numbers and longer-term monitoring to show the way endothelial cell loss develops among PEX patient populations throughout time.

CONCLUSION

The results from our study verify that PEX leads to juxtaposition of significant endothelial cell count diminution. The connection between PEX and factors including patient age combined with intraocular pressure along with chances of endothelial decompensation post intra ocular surgery supports the necessity for vigilant corneal health assessment in PEX patients particularly those with increased intraocular pressure or glaucoma. Early intervention with detection techniques becomes vital because our study reveals that this patient group requires immediate care to safeguard corneal endothelial performance.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

WRB & SAHN: Data acquisition, data analysis, critical review, approval of the final version to be published.

FH & AA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

TAK & HSR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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