International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 8, 2025
https://theaspd.com/index.php

Corneal Endothelial Changes Following Phacoemulsification In Pseudoexfoliation Syndrome: A Prospective Study

[1]**Dr. Hithesh Isukapalli, *[2]Dr. Sangeetha T**
[1]Junior Resident, Department of Ophthalmology, Sri Devaraj Urs Medical College, Kolar, India, hithesh.isukapalli20599@gmail.com
[2]Professor, Department of Ophthalmology, Sri Devaraj Urs Medical College, Kolar, India

Abstract

Background: *Pseudoexfoliation syndrome (PXF) is an age-related fibrillopathy associated with corneal endothelial vulnerability, increasing the risk of cell loss during phacoemulsification. This study evaluates corneal endothelial changes following phacoemulsification in PXF patients.*

Methods: *A prospective interventional study was conducted at R.L. Jalappa Hospital, Kolar, India, involving 25 cataract patients associated with PXF undergoing phacoemulsification. Preoperative and postoperative (Day 1, Week 1, Month 1, Month 3) assessments of ECD, pleomorphism, polymegathism, and CCT were performed using specular microscopy and ultrasound pachymetry respectively. Paired t-tests analysed changes, with significance set at $p<0.05$.*

Results: *Mean preoperative ECD was 2057.6±259.5 cells/mm², decreasing significantly to 1785.8±270.4 cells/mm² by 3rd month (13.2% loss, $p<0.001$). Pleomorphism declined from 55.2±2.6% to 51.4±2.7% ($p<0.001$), while polymegathism increased from 34.3±2.7% to 38.5±2.6% ($p<0.001$). CCT increased significantly on Day 1 (551.8±11.4 µm vs. 526.4±11.1 µm preoperatively, $p<0.001$) but normalized by 3rd month (526.4±11.1 µm, $p>0.05$). No significant intraoperative complications were reported.*

Conclusion: *Phacoemulsification in PXF patients results in significant corneal endothelial changes indicating persistent stress. Transient CCT elevation resolved by 3 months, suggesting partial functional recovery. Preoperative specular microscopy and intraoperative protective strategies are crucial to minimize endothelial damage and optimize visual outcomes.*

Keywords: *Central corneal thickness, Corneal endothelium, Cell count, Phacoemulsification, Specular microscopy*

INTRODUCTION

Pseudoexfoliation syndrome (PXF), first described by Lindberg in 1971 is an age-related systemic fibrillopathy characterized by abnormal fibrillar deposits in ocular and extraocular tissues.[1] It mainly affects anterior segment structures (corneal endothelium, lens zonules, trabecular meshwork), leading to secondary open-angle glaucoma and higher surgical risk in cataract surgery.[2] The deposits, composed of elastin-associated microfibrils, glycoproteins, and fibrillin-1, are produced by cells like the ciliary and lens epithelium.[3]

PXF prevalence varies globally, reaching up to 30% in Scandinavians over 60 and 6–18% in India, influenced by age, LOXL1 gene polymorphisms, and UV exposure.[4] Cataracts in PXF eyes are commonly associated with nuclear sclerosis, zonular weakness, poor mydriasis, and iris atrophy, increasing intraoperative risks such as zonular dialysis and capsular rupture.[5]

The corneal endothelium maintains corneal clarity via pump function but is vulnerable in PXF due to pseudoexfoliative material (PXM) deposition and altered aqueous humor with oxidative stress and inflammation.[6,7] Specular microscopy shows reduced endothelial cell density (ECD), increased polymegathism (cell size variability), and decreased pleomorphism (hexagonality) in PXF eyes.[8,9]

In PXF, phacoemulsification increases endothelial risk due to higher energy use, chamber instability, and surgical manipulation; despite modern protective techniques, postoperative endothelial cell loss remains greater than in non-PXF eyes.[10-12] Hence, this study aims to evaluate corneal endothelial changes and central corneal thickness (CCT) following phacoemulsification in PXF patients.

MATERIALS AND METHODS

This prospective interventional study was conducted at R.L. Jalappa Hospital and Research Centre, Kolar, India, from May 2023 to November 2024, following approval from the Institutional Ethics Committee and written informed consent from all participants.

Twenty-five patients aged ≥50 years with PXF and senile cataracts undergoing phacoemulsification were included while patients with history of prior ocular trauma or surgery, corneal dystrophies, pre-existing

endothelial dysfunction, uveitis, uncontrolled glaucoma, or retinal abnormalities affecting visual acuity were excluded. All patients underwent thorough ophthalmic evaluation for visual acuity, intraocular pressure, anterior and posterior segment structures. PXF was diagnosed based on slit-lamp biomicroscopy identifying characteristic fibrillar deposits on the anterior lens capsule or pupillary margin.

Following this Specular Microscopy was performed using a non-contact specular microscope (Topcon SP-1P) to measure ECD (cells/mm²), pleomorphism (% hexagonal cells), and polymegathism (coefficient of variation in cell size) and Central Corneal Thickness (CCT) by ultrasound pachymetry (PachPen, Accutome). Additionally, biometry and systemic investigations were also performed.

Phacoemulsification was performed under topical or peribulbar anaesthesia using a standard technique (Zeiss Visalis 500 phaco machine) with dispersive viscoelastic agent (Viscoat) to protect the endothelium. Cumulative dissipated energy (CDE) and fluid volume were recorded. Surgical adjuncts (e.g., iris hooks, capsular tension rings) were used as needed to manage poor pupil dilation or zonular instability. Patients were followed up on day 1, 7, 30 and 90 to assess BCVA, IOP, any postoperative complications, specular microscopy parameters (ECD, pleomorphism, polymegathism) and CCT.

Statistical Analysis

Data were analysed using SPSS (version 25.0). Descriptive statistics (means, standard deviations) summarized endothelial parameters. Paired t-tests compared preoperative and postoperative values at each time point, with significance set at $p<0.05$. Statistical test used to compare the phaco parameters between PXR and non PXF group is Independent Samples t-test (Welch's correction for unequal variances).

RESULTS

Demographic and Clinical Characteristics

The study included 25 patients with mean age of 65.4±7.2 years, IOP 16.8±2.4 mmHg and male preponderance (60%). All had PXF with nuclear or corticonuclear cataracts (grade II–IV per LOCS III classification). Mean postoperative BCVA improved from 0.8±0.3 log MAR preoperatively to 0.2±0.1 log MAR at Month 3 ($p<0.001$). No significant intraoperative complications were reported whereas transient corneal oedema was noted in 4 patients (16%) on day 1 which resolved by day 7 and mild iritis in 2 patients (8%) both managed with on postoperative medications.

Corneal endothelial changes

A statistically significant reduction in endothelial cell density (ECD) was observed postoperatively at all follow-up points compared to baseline. The mean preoperative ECD was 2057.6 ± 259.5 cells/mm². This declined to 1914.0 ± 261.4 cells/mm² on Day 1 ($t = 42.42$, $p < 0.001$), 1867.8 ± 265.3 cells/mm² at Week 1 ($t = 39.79$, $p < 0.001$), 1816.4 ± 266.5 cells/mm² at Month 1 ($t = 42.15$, $p < 0.001$), and 1785.8 ± 270.4 cells/mm² at Month 3 ($t = 45.11$, $p < 0.001$). The greatest decline was noted between the preoperative and 3-month values, indicating a progressive and sustained endothelial cell loss. [Table 1]

Pleomorphism, measured as the proportion of hexagonal cells, also demonstrated a significant postoperative reduction. The preoperative value of 55.2 ± 2.6% decreased to 52.4 ± 2.7% on Day 1 ($t = 24.08$, $p < 0.001$), followed by a further decline to 51.4 ± 2.7% at Week 1 ($t = 33.95$, $p < 0.001$), which persisted at Month 1 ($t = 33.95$, $p < 0.001$) and Month 3 ($t = 33.95$, $p < 0.001$). [Table 1]

In contrast, polymegathism showed a significant postoperative increase. The mean preoperative value of 34.3 ± 2.7% rose to 37.5 ± 2.6% on Day 1 ($t = -34.12$, $p < 0.001$), and further to 38.5 ± 2.6% at Week 1 ($t = -43.93$, $p < 0.001$). This increase was maintained at Month 1 ($t = -43.93$, $p < 0.001$) and Month 3 ($t = -43.93$, $p < 0.001$). [Table 1]

Collectively, these findings demonstrate a progressive decline in endothelial cell density and pleomorphism, accompanied by a sustained increase in polymegathism during the 3-month postoperative follow-up.

Corneal parameters	Timepoint	Mean ± SD	t-statistic	p-value
Endothelial cell density (cells/mm$^{2)}$	Pre-op	2057.6 ± 259.5	-	-
	Day 1	1914.0 ± 261.4	42.42	<0.001
	Week 1	1867.8 ± 265.3	39.79	<0.001
	Month 1	1816.4 ± 266.5	42.15	<0.001
	Month 3	1785.8 ± 270.4	45.11	<0.001
Pleomorphism (% Hexagonal Cells)	Pre-op	55.2 ± 2.6	-	-
	Day 1	52.4 ± 2.7	24.08	<0.001
	Week 1	51.4 ± 2.7	33.95	<0.001

	Month 1	51.4 ± 2.7	33.95	<0.001
	Month 3	51.4 ± 2.7	33.95	<0.001
Polymegathism (%)	Pre-op	34.3 ± 2.7	-	-
	Day 1	37.5 ± 2.6	-34.12	<0.001
	Week 1	38.5 ± 2.6	-43.93	<0.001
	Month 1	38.5 ± 2.6	-43.93	<0.001
	Month 3	38.5 ± 2.6	-43.93	<0.001

Table 1: Comparison of preoperative and postoperative corneal changes

Central Corneal Thickness (CCT)

Central corneal thickness (CCT) showed a transient postoperative increase which gradually resolved to baseline by 3 months. The mean preoperative CCT was 526.4 ± 11.1 µm. On Day 1, there was a significant increase to 551.8 ± 11.4 µm ($t = -40.11$, $p < 0.001$). By Week 1, CCT decreased to 538.6 ± 11.6 µm but remained significantly higher than baseline ($t = -42.22$, $p < 0.001$). At Month 1, CCT further decreased to 532.4 ± 11.5 µm, still significantly elevated compared to preoperative values ($t = -24.35$, $p < 0.001$). By Month 3, CCT returned to baseline levels (526.4 ± 11.1 µm) with no statistically significant difference from preoperative values ($p > 0.05$). [Table 2]]

Timepoint	Mean ± SD (µm)	t-statistic	p-value
Pre-op	526.4 ± 11.1	-	-
Day 1	551.8 ± 11.4	-40.11	<0.001
Week 1	538.6 ± 11.6	-42.22	<0.001
Month 1	532.4 ± 11.5	-24.35	<0.001
Month 3	526.4 ± 11.1	-	>0.05

Table 2: Comparison of preoperative and postoperative CCT (µm)

Phaco parameters

PXF group showed a significantly higher Mean Phaco Time (1.50 ± 0.41 s) and Effective Phaco Time (24.21 ± 9.51 s) compared to non PXF group (1.23 ± 0.48 s and 19.64 ± 10.49 s, respectively), with $p = 0.0087$ and $p = 0.0454$. Mean Phaco Power was comparable between groups (26.11 ± 3.81% vs. 25.48 ± 4.12%, $p = 0.4809$). This suggests that non PXF group achieved greater surgical efficiency with similar energy use. [Table 3]

Phaco parameters	PXF group	Non PXF group	P value	Significance
	Mean ± SD	Mean ± SD		
Phaco time	1.50 ± 0.41	1.23 ± 0.48	0.0087	Significant
Phaco power	26.11 ± 3.81	25.48 ± 4.12	0.4809	Not significant
Effective phaco time	24.21 ± 9.51	19.64 ± 10.49	0.0454	Significant

Table 3: Comparison of phaco parameters between PXF and non PXF patients

DISCUSSION

The study included 25 PXF patients (mean age 65.4 ± 7.2 years; IOP 16.8 ± 2.4 mmHg; 60% male) with grade II–IV nuclear or corticonuclear cataracts (LOCS III). Mean BCVA improved from 0.8 ± 0.3 to 0.2 ± 0.1 logMAR at 3 months ($p < 0.001$). No major intraoperative complications occurred; transient corneal edema (16%) resolved by day 7, and mild iritis (8%) responded to medication. In a prospective MSICS study of 152 PXF eyes, Day 1 clinically significant corneal edema occurred in ~ 15.1 % of eyes and mean BCVA improved from ~ 0.26 to ~ 0.07 logMAR by 3 months; intraoperative complications included zonular dialysis in 3.3 % and posterior capsular rupture in 0.7 % of cases.[13]

Similarly, in a large 8-year retrospective analysis of 12,992 eyes, pseudoexfoliation was associated with 2.68× higher odds of intraoperative complications (principally vitreous loss / zonular dehiscence), although posterior capsule rupture rates were not significantly different, and postoperative corneal decompensation was rare.[14] Compared to those, the present study's zero intraoperative complications and only transient edema (16 %) and mild iritis (8 %) are on the lower side of complication rates, likely reflecting small sample, mild disease, and meticulous surgical technique.

In the present study, a statistically significant and progressive reduction in ECD was observed, with a mean decrease of approximately 13.2% at 3 months postoperatively. Our baseline ECD (2057.6 ± 259.5

cells/mm²) was somewhat lower possibly reflecting a more advanced disease stage or demographic variation. The observed reduction in hexagonality and corresponding increase in polymegathism demonstrate postoperative morphological alterations in corneal endothelial cells, reflecting surgical stress and compensatory cellular remodelling. The sustained decline in ECD observed up to 3 months in our cohort suggests ongoing endothelial remodelling beyond the early postoperative period, underscoring the need for meticulous intraoperative management and close postoperative monitoring in PEX patients.

A study followed 61 eyes (19 with DM+PEX, 22 diabetic only, 20 PEX only) for up to six months post-op, and found that the DM+PEX group had more pronounced reductions in ECD and hexagonality and greater increases in coefficient of variation (CV) and central corneal thickness (CCT) than PEX-only or diabetic-only groups.[15]

Long-term (7-year) study in patients post-phacoemulsification, showing that although early postoperative differences in endothelial cell count (ECC) and morphology are seen depending on initial corneal swelling, over 7 years, many of these differences converge towards a steady state. Useful for comparison of your 3-month results with long-term trends.[16]

Another study comprising of 62 PEX eyes and 62 control eyes, with follow up at 6 months, 1 year, and 2 years, preop ECDs were ~2258 ± 342 for PEX and ~2322 ± 321 for non-PEX; shows long-term cell density loss with gradual decline.[17]

Postoperatively, mean endothelial cell loss (7.7–12.4%) was comparable between PXF and control groups, with no cases of corneal edema. Transient polymegethism and pleomorphism were observed early after surgery, stabilizing within six months, although PXF eyes exhibited slightly slower endothelial remodeling.[18] Application of a dispersive viscoelastic agent (Viscoat) appears to have mitigated further endothelial cell density loss in high-risk eyes.[19]

CCT elevation on Day 1 (551.8 μm) reflects transient endothelial pump dysfunction, consistent with Arvind et al.'s observation of prolonged CCT elevation in PXF eyes compared to controls.[20] The return to baseline by Month 3 indicates functional recovery, aligning with Hayashi K et al.'s findings.[21] However, persistent morphological changes (increased polymegathism, reduced pleomorphism) suggest ongoing subclinical stress, potentially increasing long-term decompensation risk.

The increased endothelial susceptibility in PXF may stem from oxidative stress and inflammatory mediators in the aqueous humour, including elevated IL-6, TNF-α, and matrix metalloproteinases (MMP-2, MMP-9), as reported by Borra T et al.[22] These factors impair endothelial metabolism and pump efficiency, exacerbating surgical trauma.

The absence of significant intraoperative complications in this study may be attributed to controlled phaco energy (mean CDE 8.5±2.3) and the use of capsular tension rings in 20% of cases to stabilize zonular weakness. However, higher CDE in denser cataracts, common in PXF, correlates with greater ECD loss, as noted by Hayashi K et al.[21] Optimizing phaco settings (e.g., torsional ultrasound) could further reduce endothelial trauma.

While specular microscopy provided robust data, in vivo confocal microscopy could offer deeper insights into subclinical endothelial changes, such as guttae or irregular cell borders, as suggested by Martone G et al.[23] Integrating confocal imaging pre and post-surgery could enhance risk stratification and long-term monitoring in PXF patients.

The significant ECD loss and morphological changes underscore the need for routine preoperative specular microscopy in PXF patients to assess baseline endothelial health. Postoperative monitoring beyond 3 months is critical to detect delayed decompensation.

PXF's systemic associations, including cardiovascular disease and diabetes, may exacerbate endothelial vulnerability, as noted by Andrikopoulos GK et al.[24] In this study, 28% of patients had controlled diabetes, potentially contributing to endothelial stress.

Limitations

This study has certain limitations. First, the small sample size (n = 25) and single-center design restrict generalizability, underscoring the need for larger multicenter studies. Second, the absence of a non-PXF control group limits attribution of changes specifically to PXF pathology. Furthermore, the relatively short follow-up period of 3 months may not capture delayed endothelial decompensation. Finally, variability in surgical technique and cataract density could have influenced the outcomes.

CONCLUSION

Phacoemulsification in PXF patients results in significant endothelial cell loss, increased polymegathism, and reduced pleomorphism, reflecting persistent endothelial stress. Transient CCT elevation resolves by 3 months, indicating partial functional recovery. These findings highlight the need for preoperative specular microscopy, intraoperative protective strategies (e.g., dispersive viscoelastics, low-energy phaco), and vigilant postoperative monitoring to optimize visual outcomes.

REFERENCES

1. Lindberg JG. Clinical investigations on depigmentation of the pupillary border and translucency of the iris in cases of senile cataract and in normal eyes in elderly persons. Acta Ophthalmol Suppl (1985). 1989;190:1-96. PMID: 2541596.
2. Ritch R, Schlotzer-Schrehardt U. Exfoliation syndrome. Surv Ophthalmol. 2001;45(45): 265-315. PMID: 11166342.
3. Schlotzer-Schrehardt U, Naumann GO. A histopathologic study of zonular instability in pseudoexfoliation syndrome. Am J Ophthalmol. 1994;118(6):730-43. PMID: 7977599.
4. Schlotzer – Schrehardt U. Molecular pathology of pseudoexfoliation syndrome/glaucoma–new insights from LOXL1 gene associations. Exp Eye Res. 2009;88(4):776-85. PMID: 18809397.
5. Pasutto F, Krumbiegel M, Mardin CY, Paoli D, Lammer R, Weber BH, et, al. Association of LOXL1 common sequence variants in German and Italian patients with pseudoexfoliation syndrome and pseudoexfoliation glaucoma. Invest Ophthalmol Vis Sci. 2008;49(4):1459-63. PMID: 18385063.
6. Erkayhan GE, Dogan S. Cataract Surgery and Possible Complications in Patients with Pseudoexfoliation Syndrome. Eurasian J Med. 2017;49(1):22-25. PMID: 28416927.
7. Bourne WM. Biology of the corneal endothelium in health and disease. Eye (Lond). 2003;17(8):912-8. PMID: 14631396.
8. Aydin Yaz Y, Yildırım N, Yaz Y, Tekin N, Inal M, Sahin FM. Role of Oxidative Stress in Pseudoexfoliation Syndrome and Pseudoexfoliation Glaucoma. Turk J Ophthalmol. 2019;49(2):61-67. PMID: 31055889
9. Miyake K, Matsuda M, Inaba M. Corneal endothelial changes in pseudoexfoliation syndrome. Am J Ophthalmol. 1989;108(1):49-52. PMID: 2750833.
10. Hayashi K, Hayashi H, Nakao F, Hayashi F. Risk factors for corneal endothelial injury during phacoemulsification. J Cataract Refract Surg. 1996;22(8):1079-84. PMID: 8915805.
11. Tekin K, Inanc M, Elgin U. Monitoring and management of the patient with pseudoexfoliation syndrome: current perspectives. Clin Ophthalmol. 2019 Mar 1;13:453-464. PMID: 30880906
12. Jammal H, Abu Ameera M, Al Qudah N, Aldalaykeh M, Abukahel A, Al Amer A, Al Bdour M. Characteristics of Patients with Pseudoexfoliation Syndrome at a Tertiary Eye Care Center in Jordan: A Retrospective Chart Review. Ophthalmol Ther. 2021;10(1):51-61. PMID: 33123988
13. Shivkumar C, Gadiwan M, Rout M, Ghosh A, Haroon S, Ramakrishnan R. Visual outcomes and complications of manual small-incision cataract surgery in patients with pseudoexfoliation. Indian J Ophthalmol. 2022;70(11):3912-3917. PMID: 36308126
14. Thevi T, Abas AL. Intraoperative and postoperative complications of cataract surgery in eyes with pseudoexfoliation - An 8-year analysis. Oman J Ophthalmol. 2019;12(3):160-165. PMID: 31902990
15. Mahmoud, M.SD., Omar, I.A.N. & AttaAllah, H.R. Evaluation of the corneal thickness and endothelial changes following uncomplicated phacoemulsification in diabetic and non-diabetic patients with pseudo-exfoliation syndrome by specular microscopy. Int Ophthalmol 43, 4773–4780 (2023). https://doi.org/10.1007/s10792-023-02877-x
16. Lundberg, B. Corneal endothelial changes seven years after phacoemulsification cataract surgery. Int Ophthalmol 44, 169 (2024). https://doi.org/10.1007/s10792-024-03044-6
17. Kristianslund O, Pathak M, Østern AE, Drolsum L. Corneal endothelial cell loss following cataract surgery in patients with pseudoexfoliation syndrome: a 2-year prospective comparative study. Acta Ophthalmol. 2020;98(4):337-342. PMID: 31773906.
18. Wirbelauer C, Anders N, Pham DT, Wollensak J. Corneal Endothelial Cell Changes in Pseudoexfoliation Syndrome After Cataract Surgery. Arch Ophthalmol. 1998;116(2):145–149. doi:10.1001/archopht.116.2.145
19. Borkenstein AF, Borkenstein EM, Malyugin B. Ophthalmic Viscosurgical Devices (OVDs) in Challenging Cases: a Review. Ophthalmol Ther. 2021;10(4):831-843. PMID: 34617249.
20. Arvind H, Raju P, Paul PG, Baskaran M, Ramesh SV, George RJ, McCarty C, Vijaya L. Pseudoexfoliation in South India. Br J Ophthalmol. 2003;87(11):1321-3. PMID: 14609823.
21. Hayashi K, Manabe S, Yoshimura K, Kondo H. Corneal endothelial damage after cataract surgery in eyes with pseudoexfoliation syndrome. J Cataract Refract Surg. 2013;39(6):881-7. PMID: 23582364.
22. Borras T. Growth Factors, Oxidative Damage, and Inflammation in Exfoliation Syndrome. J Glaucoma. 2018;27(1):S54-S60. PMID: 29401156.
23. Martone G, Casprini F, Traversi C, Lepri F, Pichierri F, Caporossi A. Pseudoexfoliation syndrome: in vivo confocal microscopy analysis. Clin Exp Ophthalmol. 2007;35(6):582-585. doi.org/10.1111/j.1442-9071.2007.01535.x
24. Andrikopoulos GK, Alexopoulos DK, Gartaganis SP. Pseudoexfoliation syndrome and cardiovascular diseases. World J Cardiol. 2014;6(8):847-54. PMID: 25228963