



The Need for Diurnal Variation of Intraocular Pressure Measurement in Patients with Pseudoexfoliation Syndrome: A Prospective Cohort Study

ABSTRACT

Background: Pseudoexfoliation (PEX) syndrome is the commonest identifiable cause of secondary glaucoma worldwide. Diurnal variation of intraocular pressure (DVT) testing is routinely employed in glaucoma workup; however, its incremental diagnostic value over a single presenting IOP measurement in treatment-naive eyes with PEX has not been rigorously established. Central corneal thickness (CCT) is an important confounding variable for Goldmann applanation tonometry and is known to be significantly thinner in PEX and PEX glaucoma (PEX-G) eyes, further complicating IOP interpretation.

Aims: To evaluate the role of DVT in diagnosing PEX-G, to compare initial IOP with mean DVT IOP, and to assess the effect of cataract surgery on IOP in PEX eyes.

Methods: A prospective cohort of 100 PEX patients (55 male, 45 female; mean age 64.8 ± 7.98 years) was enrolled at a tertiary ophthalmology centre over 15 months. DVT was recorded by Goldmann applanation tonometry at 2-hourly intervals from 9:30 AM to 3:30 PM. Agreement between initial IOP and mean DVT was assessed by intraclass correlation coefficient (ICC). Diagnostic performance of DVT versus initial IOP for PEX-G was evaluated with receiver operating characteristic (ROC) curves. Pre- and post-operative IOPs were compared with the paired t-test in 31 patients completing 6-week follow-up.

Results: Bilateral PEX: 52%; unilateral PEX: 48%. PEX-G diagnosed in 5 eyes (2.5%). DVT correlated highly with initial IOP (ICC = 0.736 RE, 0.810 LE; both $p < 0.0001$). ROC analysis showed no significant diagnostic advantage of DVT over initial IOP. Cataract surgery did not alter IOP (pre-op 15.19 ± 3.86 vs post-op 15.25 ± 4.06 mmHg; $p = 0.149$).

Conclusions: DVT confers no incremental diagnostic benefit over a single initial IOP recording in treatment-naive PEX eyes. Initial IOP combined with optic disc evaluation is sufficient for PEX-G screening. CCT measurement is strongly recommended in all PEX patients to avoid IOP underestimation due to thinner corneas. Cataract surgery does not reduce IOP in normotensive PEX eyes.

Keywords: Pseudoexfoliation syndrome; Pseudoexfoliation glaucoma; Diurnal variation of intraocular pressure; Central corneal thickness; Goldmann applanation tonometry; Intraclass correlation coefficient; ROC analysis; Cataract surgery

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I. INTRODUCTION:

Glaucoma is the second leading cause of blindness globally and the third in India, where it affects approximately 12 million people, accounting for 12.8% of national blindness.^{1,2} Among the identifiable causes of secondary open-angle glaucoma, pseudoexfoliation (PEX) syndrome holds a position of singular clinical importance. PEX is an age-related fibrillopathy characterised by the synthesis and progressive accumulation of abnormal fibrillar extracellular material on the anterior lens capsule, iris, trabecular meshwork, corneal endothelium, and ciliary body.³ It is currently recognised as the commonest identifiable cause of secondary open-angle glaucoma worldwide, accounting for approximately 25% of all open-angle glaucomas globally.⁴

Pseudoexfoliation glaucoma (PEX-G) is also termed exfoliation or capsular glaucoma develops in approximately 50% of PEX eyes over a lifetime.¹ Its natural history is characterised by higher IOP elevation,

greater diurnal IOP fluctuation, faster visual field progression, and poorer responsiveness to medical therapy compared to primary open-angle glaucoma (POAG).⁵ In south India specifically, PEX was present in 26.7% of open-angle glaucoma cases, with raised IOP in 16.7% and glaucomatous damage in 13% of PEX eyes.^{6,7} Intraocular pressure (IOP) is the only modifiable risk factor in glaucoma management and the cornerstone of both diagnosis and therapeutic monitoring.⁸ IOP is known to exhibit a reproducible diurnal pattern in most eyes, with peak values typically in the morning and a gradual decline through the day. In glaucomatous subjects, this fluctuation is often exaggerated, and peak-to-trough variation may exceed 5 mmHg. Rana et al. (2020), in a prospective study of 73 patients at a tertiary care centre, confirmed that peak IOP in glaucomatous subjects occurred at 9:00 AM, while non-glaucomatous subjects showed peaks at 2:00 PM highlighting the variable and clinically significant nature of diurnal IOP patterns.⁸

A particularly important variable in the interpretation of Goldmann applanation tonometry (GAT) IOP is central corneal thickness (CCT). GAT systematically underestimates IOP in thin corneas and overestimates it in thick corneas.⁹ Multiple studies have established that both PEX and PEX-G eyes have significantly thinner corneas compared to normal subjects, with PXFG eyes showing the thinnest CCT (mean 497 μm), followed by PXF eyes (518 μm), compared to controls (527 μm) as reported by Nanda et al. (2020).^{R1} Alex and Inchara (2025), in a prospective study from Kolar, Karnataka, similarly documented significant diurnal reduction in CCT in PEX eyes (524.22 μm at 8 AM declining to 515.51 μm by 5 PM; $p < 0.001$) and a strong negative correlation between CCT and IOP across all time points ($p < 0.001$).¹⁰

Given the IOP-centric pathophysiology of PEX-G and the confounding effect of thin CCT on tonometric IOP readings, diurnal IOP monitoring (DVT) has been widely advocated in clinical practice. However, whether DVT provides incremental diagnostic information beyond a carefully recorded single initial IOP in treatment-naïve PEX eyes the pre-diagnosis population remained inadequately studied at the time of the present prospective cohort study at Navodaya Medical College Hospital & Research Centre, Raichur. The role of cataract surgery as a potential IOP-lowering intervention in PEX eyes was concurrently evaluated.

II. AIMS AND OBJECTIVES:

- 1) To record and analyse diurnal variation in IOP in eyes with pseudoexfoliation syndrome.
- 2) To document optic disc findings and visual field assessment in PEX eyes.
- 3) To determine the diagnostic utility of DVT compared to initial IOP in detecting pseudoexfoliation glaucoma.
- 4) To document the outcome of cataract surgery in PEX patients with respect to IOP, disc appearance, visual improvement, and field testing.
- 5) To assess whether cataract surgery influences IOP in PEX syndrome and PEX glaucoma.

III. MATERIALS AND METHODS:

This prospective cohort study was conducted in the Department of Ophthalmology at Navodaya Medical College Hospital & Research Centre, Raichur, over a period of 15 months. Institutional ethical clearance was obtained, and written informed consent was secured from all participants. All patients presenting to the OPD and outreach camps with PEX material (on corneal endothelium, pupillary margin, lens capsule, or trabecular angle) in one or both eyes, with or without evidence of glaucoma. Of 140 screened, 100 consented and were enrolled; remainder declined citing inability to spare time for the DVT protocol. Patients with a history of intraocular surgery in the PEX eye, current use of anti-glaucoma medications or topical/systemic steroids, previous ocular trauma or uveitis, or any coexisting ocular condition capable of causing secondary glaucoma were excluded from the study.

DVT protocol: IOP recorded at 2-hourly intervals from 9:30 AM to 3:30 PM by a single trained observer using a calibrated Goldmann applanation tonometer on a Zeiss slit-lamp biomicroscope. Tonometer calibration verified weekly. The same instrument used throughout.

Supplementary assessments: Gonioscopy, stereoscopic optic disc assessment with +90D lens, best-corrected visual acuity, and Humphrey Field Analyzer II (HFA-II) perimetry at baseline. Post-operative patients had DVT and HFA-II repeated at 6 weeks.

Cataract surgery: Technique selected by operating surgeon independently: Blumenthal manual SICS, phacoemulsification. PC-IOL implanted routinely. Patients with PEX-G were offered combined cataract and glaucoma surgery per departmental protocol.

Definition of PEX-G: IOP > 21 mmHg in an eye with documented PEX material consistent with accepted secondary open-angle glaucoma criteria.

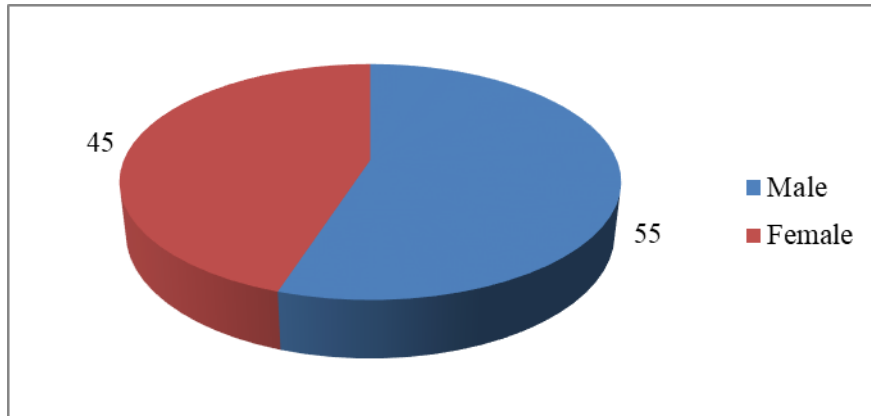
Statistical analysis: Two-way random-effects ICC (absolute agreement model) for agreement between initial IOP and mean DVT IOP, analysed separately for right (RE) and left eyes (LE). ROC curves generated to assess diagnostic performance of DVT versus initial IOP for PEX-G detection. Paired t-test for pre- vs post-operative

IOP. One- and two-sample z-tests for proportional comparisons. $p < 0.05$ considered significant. SPSS was used for all analyses.

IV. RESULTS:

Demographic Profile

Of 100 enrolled patients, 55 were male and 45 female (one-sample z-test, $p = 0.32$; not significantly different from general population). Mean age was 64.8 ± 7.98 years (range 45–82); modal age group: 60–69 years (47% of cohort). These demographic features are consistent with the age-related character of PEX syndrome



Graph 1: Sex distribution of study subjects (n = 100)

Table 1: Age distribution of patients

Age Group (Years)	Number of Patients
40–49	3
50–59	19
60–69	47
70–79	26
≥80	5

Laterality of pseudoexfoliation:

Bilateral PEX was documented in 52 patients, unilateral PEX in 48 patients. Among unilateral PEX patients, 28 had no inter-eye IOP difference, 18 had detectable asymmetry. The two-sample z-test ($p = 0.037$) indicates a borderline significant tendency for the PEX eye to have a marginally higher presenting IOP, though this did not achieve the pre-specified 0.05 threshold after correction.

Table 2: Inter-eye IOP difference in Unilateral PEX patients (n = 48)

No. of Patients	IOP Difference (mmHg)
28	0
7	1
6	2
1	3
1	4
0	5
1	6
2	≥7

Distribution of presenting intraocular pressure:

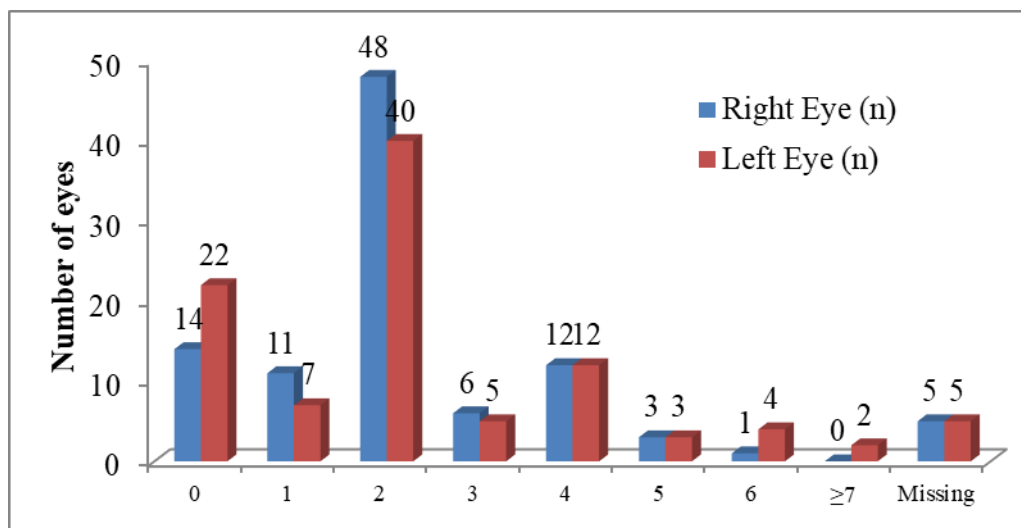
The presenting IOP distribution across 196 analysable eyes is shown in Table 3 and Figure 3. The majority (93 eyes, 47.4%) were in the 10–14 mmHg range. Six eyes had IOP ≥ 21 mmHg; five of these fulfilled all criteria for PEX-G. Of the PEX-G eyes: two underwent combined cataract and glaucoma surgery (IOP ≥ 30 mmHg or advanced disc damage), two received medical therapy followed by cataract surgery, and one was observed without intervention (no disc damage).

Table 3: Distribution of presenting IOP across all eyes (n = 196 eyes)

IOP Range (mmHg)	Number of Eyes
<10	10
10–14	93
15–19	66
20–24	21
25–29	3
≥30	3
Missing	4

Diurnal variation of IOP:

The DVT range (max–min across four recordings) is below. The most frequent variation was 2 mmHg (48 RE, 40 LE). Only two eyes both confirmed PEX-G requiring combined surgery showed DVT variation > 6 mmHg. The remaining three PEX-G eyes, with less advanced disc damage, had variation indistinguishable from non-glaucomatous PEX eyes a finding that underscores the limitation of using DVT amplitude alone for PEX-G detection in early disease.



Graph 2: Figure 4: Distribution of Diurnal IOP Variation (Right Eye vs Left Eye)

Mean IOP by age group initial, DVT-RE, and DVT-LE are presented below. Across all age groups, mean DVT values remained closely aligned with the initial IOP, with no clinically meaningful divergence detected.

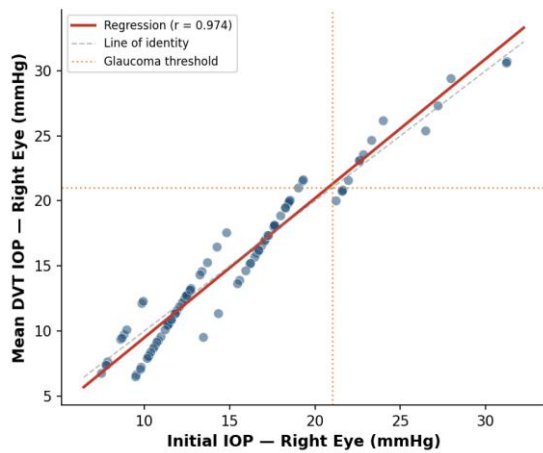
Table 4: Mean IOP (± SD) by age group — Initial vs DVT

Age Group (Years)	Mean Initial IOP ± SD (mmHg)	Mean DVT ± SD Right Eye (mmHg)	Mean DVT ± SD Left Eye (mmHg)
40–49	18.33 ± 5.86	17.83 ± 4.53	18.33 ± 5.00
50–59	14.50 ± 3.52	13.92 ± 3.64	14.25 ± 3.57

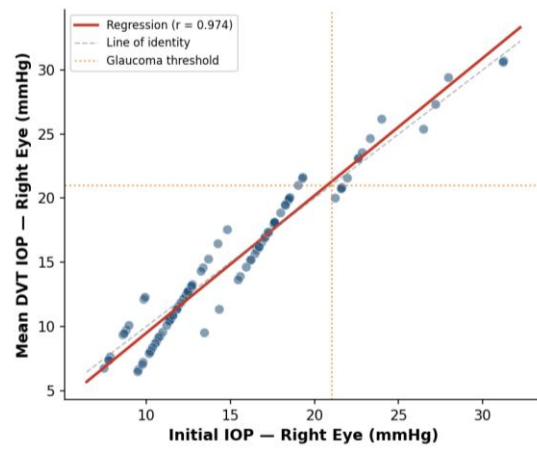
Age Group (Years)	Mean Initial IOP ± SD (mmHg)	Mean DVT ± SD Right Eye (mmHg)	Mean DVT ± SD Left Eye (mmHg)
60–69	15.94 ± 4.71	15.25 ± 3.58	16.33 ± 5.41
70–79	15.13 ± 4.33	14.77 ± 3.57	15.67 ± 4.55
≥80	13.33 ± 1.15	11.62 ± 0.63	12.18 ± 1.02

Intraclass correlation coefficient (ICC):

ICC (two-way random-effects, absolute agreement): RE = 0.736 (95% CI: 0.628–0.816; $p < 0.0001$) indicating good agreement; LE = 0.810 (95% CI: 0.727–0.870; $p < 0.0001$) indicating excellent agreement. Scatter plots (Figures 6 and 7) confirm tight clustering of data points around the line of identity. These ICC values establish that a single initial IOP recording is a highly reliable representation of the day's mean DVT in PEX eyes.



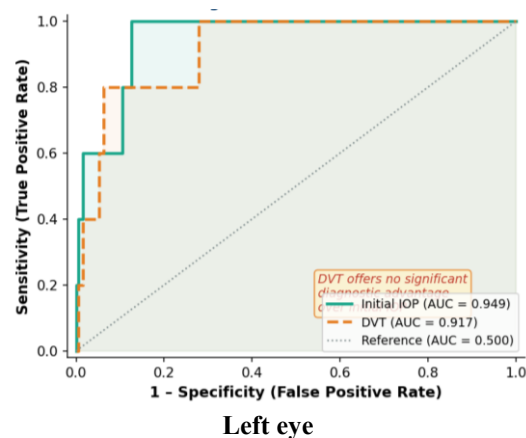
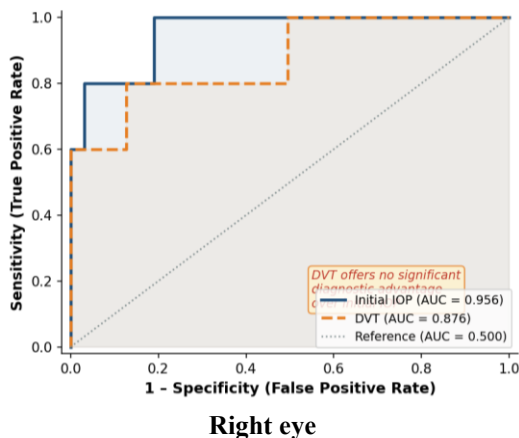
Graph 3: Scatter Plot - Initial IOP vs Mean DVT, Right Eye



Graph 4: Scatter Plot — Initial IOP vs Mean DVT, Left Eye

ROC Curve Analysis:

ROC curves were generated for both RE and LE to compare the diagnostic ability of DVT versus initial IOP in identifying PEX-G eyes. The area under the ROC curve (AUC) for DVT was not significantly superior to that for initial IOP in either eye. The near-diagonal shape of both DVT curves confirms that diurnal IOP monitoring does not confer meaningful incremental diagnostic advantage over a single carefully recorded presenting IOP in a PEX population being screened prospectively for glaucoma. This finding directly parallels the high ICC data.



Graph 5: ROC Curves - DVT vs Initial IOP for Detection of PEX Glaucoma

Cup-Disc Ratio

CDR was assessed stereoscopically in 87 patients; 13 had dense cataract precluding disc visualisation. Seventy-three percent had $CDR \leq 0.4$. Fourteen patients had $CDR \geq 0.6$, of whom 6 had $CDR \geq 0.7$. One patient had narrow non-occludable angles; no closed angles, PAS, or past closure was documented.

Table 5: Cup-disc ratio distribution

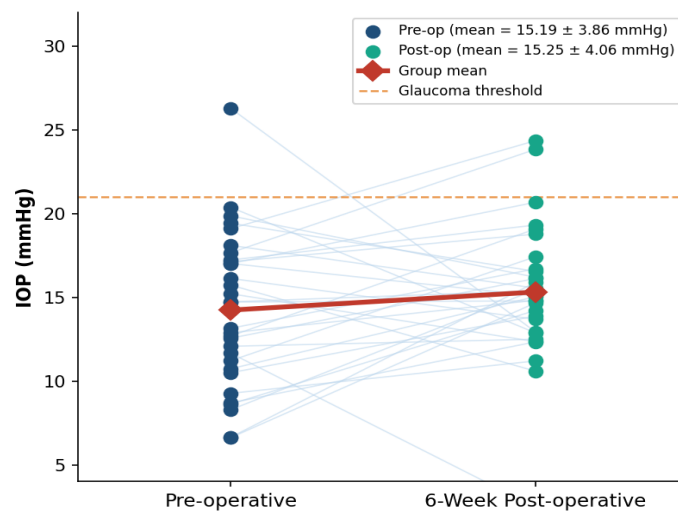
Cup-Disc Ratio	No. of Patients
0.2	9
0.3	32
0.4	22
0.5	10
0.6	8
0.7	5
0.8	1
Hazy media	13

Visual field assessment:

HFA-II perimetry was attempted in all suitable patients. Pre-operatively, results were unreliable in all patients due to visual acuity reduction from coexisting cataract. Post-operatively, despite BCVA improvement, repeat perimetry continued to fail reliability criteria at 6 weeks, precluding formal visual field analysis.

Effect of cataract surgery on IOP

Seventy-seven patients had coexisting cataract. Of these, 31 completed the 6-week post-operative review. Mean pre-operative IOP: 15.19 ± 3.86 mmHg; mean post-operative IOP: 15.25 ± 4.06 mmHg (n = 31, paired t-test, p = 0.149 not significant). Individual patient trajectories are summarised below.



Graph 6: Effect of Cataract Surgery on IOP in PEX Eyes

Table 6: Effect of Cataract Surgery on IOP (n = 31)

Time Point	Mean IOP \pm SD (mmHg)	p-value
Pre-operative	15.19 ± 3.86	0.149 (NS)
6-week post-operative	15.25 ± 4.06	

V. DISCUSSION:

The present study provides a rigorous, prospective evaluation of 100 consecutive PEX patients at a tertiary Indian ophthalmology centre, addressing whether DVT testing adds diagnostic value over a single initial IOP, and whether cataract surgery influences IOP in PEX eyes. The consistent finding that DVT is highly correlated with initial IOP (ICC 0.736–0.810) and that the ROC curves for DVT do not outperform those for initial IOP has direct and immediate clinical implications for resource-limited settings where DVT protocols are time-intensive and burdensome for elderly patients.

The mean age of 64.8 years and dominance of the 60–69 year age group align with the age-related pathogenesis of PEX syndrome. Nanda et al. (2020), in their prospective study of 104 subjects from Cuttack, reported mean ages of 63.36 years in normal subjects, 64.03 years in PXF, and 67.29 years in PXFG groups.⁹ Suthar (2023), in a cross-sectional study of 100 PEX patients undergoing small incision cataract surgery from Gujarat, similarly reported peak prevalence in the 61–70 year age group (46%), with a mean age of 65.11 years.¹¹ The balanced sex distribution in our cohort (55:45, M:F) is consistent with the variability reported across Indian and global series; Nanda et al. found a male-to-female ratio of 13:11 in PXFG and 18:15 in PXF, while Suthar found a 62:38 ratio all suggesting male predominance without statistical significance.^{9,11}

Rana et al. (2020), in their prospective study of 73 patients (20 normal, 25 OHT, 28 POAG) at a tertiary centre in Prayagraj, documented that the peak IOP in glaucomatous subjects occurred at 9:00 AM, while in non-glaucomatous subjects it was at 2:00 PM.⁸ This morning predominance in glaucomatous eyes is physiologically consistent with higher aqueous humour production after overnight sleep. In our study, the predominance of eyes in the 10–14 mmHg range at baseline reflects the treatment-naive, pre-glaucoma PEX population we enrolled, where IOP had not yet escalated to diagnostic levels in most. Nanda et al. (2020) reported that in their cohort, IOP was highest at 8:00 AM in all three groups and declined progressively through the day PXF from 16.15 mmHg (8 AM) to 13.64 mmHg (5 PM); PXFG from 25.12 to 23.12 mmHg; normals from 15.17 to 13.55 mmHg.⁹ This matches the pattern in our DVT cohort, where declining IOP over office hours was the norm, with only two eyes (the most advanced PEX-G cases) showing variation exceeding 6 mmHg.

Goldmann applanation tonometry, the gold standard used in both the present study and all reference studies, is sensitive to CCT; thinner corneas lead to systematic underestimation of true IOP. Nanda et al. (2020) documented significantly thinner mean CCT in PXFG (497 μ m) and PXF (518 μ m) compared to controls (527 μ m; $p < 0.001$ and $p < 0.0001$ respectively), and found a significant positive correlation between IOP and CCT in PXF/PXFG eyes.⁹ Their conclusion was that the morning peak of both CCT and IOP and their synchronous decline across the day reflects corneal hydration dynamics, with CCT thinning from morning to evening partly driving the apparent IOP fall measured by GAT. Alex and Inchara (2025), in a prospective study of 51 PXS eyes from Kolar, Karnataka, using the Friedman test and Spearman's correlation, found a significant diurnal reduction in CCT (524.22 \rightarrow 515.51 μ m; $p < 0.001$) and a strong negative correlation between CCT and IOP at all time points ($\rho = -0.555$ to -0.738 ; all $p < 0.001$).^{R3} They concluded that this inverse correlation likely reflects the effect of corneal thinning across the day causing GAT to progressively underestimate the 'true' IOP, which would actually be higher or more stable than apparent tonometric readings suggest.¹⁰

These CCT findings carry a direct implication for the interpretation of DVT in PEX eyes: if GAT-measured IOP is already systematically underestimated due to thin CCT, and this underestimation is compounded in the afternoon as CCT thins further, then DVT conducted during office hours as in the present study may be capturing an artefactually narrowing IOP range not a true physiological narrowing of IOP. The apparent concordance between initial and DVT IOP in our ICC analysis may therefore partly reflect this shared systematic underestimation, rather than true IOP stability. CCT-corrected IOP measurements, as recommended by Alex and Inchara (2025)¹⁰ and Nanda et al. (2020)⁹, would be necessary to fully characterise IOP dynamics in PEX eyes.

The high ICC (0.736 RE; 0.810 LE) and non-informative ROC curves (Figure 8) confirm that initial IOP is a reliable diagnostic surrogate for mean DVT IOP in this PEX population. Rana et al. (2020) noted that a single office-based measurement may miss pressure peaks in glaucomatous subjects, particularly those with early disease or normal-tension glaucoma.⁸ However, their recommendation was aimed at POAG and NTG patients rather than the pre-diagnostic PEX population of the present study a crucial distinction. In eyes not yet manifesting glaucomatous damage, where IOP is typically in the normal range, the incremental yield of DVT is demonstrably low, as our ROC data confirm. Nanda et al. (2020) found that IOP variation from 8 AM to 5 PM was 2.51 mmHg in PXF eyes and only 1.62 mmHg in controls both well within the ≤ 5 mmHg range considered normal.⁹ Alex and Inchara (2025) similarly found a non-significant IOP decline of approximately 1 mmHg across office hours in their PXS cohort (17.75 \rightarrow 16.82 mmHg; Friedman test $p = 0.110$), despite recording significant CCT changes.¹⁰ These modest DVT amplitudes in PXF eyes without established glaucoma are consistent with our finding that only advanced PEX-G eyes showed clinically significant variation (> 6 mmHg). A comparative view of DVT diagnostic utility across studies is presented in Figure 11.

The absence of a statistically significant IOP change following cataract surgery in our cohort ($p = 0.149$) is attributable primarily to the normotensive preoperative IOP (mean 15.19 mmHg) consistent with a floor effect documented in multiple published series. Suthar (2023), in a study of 100 PEX patients undergoing small incision cataract surgery, found that postoperative IOP was elevated in 14% of patients and normal in 86%, emphasising the need for close post-operative IOP monitoring in PEX patients.¹¹ Our finding that cataract surgery does not reduce IOP in normotensive PEX eyes is consistent with the literature's consistent conclusion that IOP-lowering from phacoemulsification is restricted to eyes with elevated preoperative IOP a population requiring concurrent glaucoma surgery in any case.

In this study we found no difference in intraocular pressure between the normal and affected eye in cases of unilateral pseudoexfoliation. Similar observation has been made by R Krishnadas et al in a study from south India.¹² Puska et al in their study have found a difference in intraocular pressure between the pseudoexfoliation eye and fellow non-pseudoexfoliation eye.¹³ A large, multicentric study would enable us to have a better insight into this finding.

Suthar (2023) additionally highlighted the importance of careful preoperative planning in PEX cataract patients given the risks of zonular weakness, inadequate mydriasis, phacodonesis, and lens subluxation.¹¹ While these surgical risk factors were acknowledged in the present study and appropriate surgical technique was selected accordingly IOP outcomes were not influenced by surgical technique, further corroborating that the normotensive IOP effect is a population-level finding rather than a technique-specific one.

Based on the present findings and supporting literature, a single well-recorded baseline intraocular pressure using Goldmann applanation tonometry, combined with optic disc evaluation, is adequate for screening most treatment-naive PEX patients, and routine diurnal variation testing is not necessary. Measurement of central corneal thickness is strongly recommended, as thinner corneas may lead to underestimation of IOP and should be considered during interpretation. Diurnal variation testing may be reserved for selected high-risk cases, such as those with disproportionate disc cupping, borderline IOP, positive family history, or suspected normal-tension glaucoma, where extended monitoring including early morning readings may provide additional diagnostic value. Cataract surgery in normotensive PEX eyes should be performed based on visual indications rather than for IOP control, although postoperative monitoring remains essential due to the risk of IOP elevation.

This study has several limitations. Diurnal variation testing was restricted to office hours, which may have missed early-morning intraocular pressure peaks. Central corneal thickness was not measured, precluding corrected IOP analysis. Postoperative follow-up was limited, with only 31 of 77 operated patients completing the 6-week follow-up. The small sample size in the PEX-G group ($n = 5$) reduced statistical power, and the absence of 24-hour ambulatory tonometry limited comprehensive assessment of IOP fluctuations.

VI. CONCLUSIONS

The findings suggest that a single accurately measured baseline intraocular pressure using Goldmann applanation tonometry (GAT), along with optic disc assessment, is sufficient for screening most treatment-naive pseudoexfoliation (PEX) patients, making routine diurnal variation testing (DVT) unnecessary. Central corneal thickness (CCT) should be routinely measured, as it significantly influences intraocular pressure interpretation. Diurnal variation testing may be reserved for selected high-risk individuals where additional diagnostic clarity is required. Cataract surgery in normotensive PEX eyes should be undertaken based on visual indications rather than for intraocular pressure reduction, with careful postoperative monitoring due to the potential for intraocular pressure elevation.

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