

# Assessment of Central Corneal Thickness and Corneal Curvature in Patients with Pseudoexfoliation: A Cross-sectional Study

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## ABSTRACT

**Introduction:** Pseudoexfoliation Syndrome (PEX) is the most frequently reported cause of secondary open-angle glaucoma, accounting for approximately 25-30% of global cases. PXG is typically more aggressive than Primary Open-Angle Glaucoma (POAG), as evidenced by higher Intraocular Pressures (IOP), greater pressure fluctuations, and faster progression of visual field loss. Central Corneal Thickness (CCT) is a key parameter in ocular assessment for PEX patients. However, current literature offers conflicting findings regarding CCT in PEX patients.

**Aim:** The present study compared CCT and corneal curvature between individuals with and without PXF to evaluate the IOP readings in PXF patients, thereby aiding in the early detection and management of glaucoma.

**Materials and Methods:** The present hospital-based, cross-sectional, study included 53 patients with unilateral or bilateral PXF (study group) and 53 age-matched control patients without corneal pathology. CCT was measured using Anterior Segment-Optical Coherence Tomography (AS-OCT), and corneal curvature was measured using an auto refractometer.

Independent sample t-tests and paired sample t-tests were used for statistical comparisons between groups.

**Results:** The mean CCT was  $506.15 \pm 36 \mu\text{m}$  in the study group and  $501.4 \pm 34.74 \mu\text{m}$  in the control group ( $p=0.626$ ). The mean corneal curvature ( $K_1$ ) in the right eye (OD) was  $44.2 \pm 2.0 \text{ D}$  in the study group and  $45.11 \pm 2.03 \text{ D}$  in the controls ( $p=0.024$ ).  $K_2$  in OD was  $46.1 \pm 1.3 \text{ D}$  in the study group and  $46.9 \pm 1.2 \text{ D}$  in controls ( $p=0.005$ ). In the left eye (OS), the mean  $K_1$  was  $44.06 \pm 1.7 \text{ D}$  in the study group and  $45.04 \pm 1.5 \text{ D}$  in controls ( $p=0.002$ ), while the mean  $K_2$  was  $46.5 \pm 1.2 \text{ D}$  in the study group and  $47.2 \pm 1.3 \text{ D}$  in controls ( $p=0.009$ ). There was no statistically significant difference in CCT between PXF and control eyes ( $p=0.626$ ). However, keratometry values ( $K_1$  and  $K_2$ ) were significantly lower in PXF eyes compared to controls in both OD and OS.

**Conclusion:** There was no significant difference in mean CCT between the PXF and control groups, nor between PXF eyes and fellow eyes in unilateral PXF cases. However, the mean corneal curvature was significantly lower in individuals with PXF than those without, suggesting possible implications for accurate IOP measurement and early glaucoma management.

**Keywords:** Glaucoma risk assessment, Intraocular pressure, Pseudoexfoliation syndrome

## INTRODUCTION

The PEX is an age-related systemic microfibrillopathy with a significant genetic component [1]. The onset of PEX and Pseudoexfoliative Glaucoma (PXG) has been strongly associated with a Single Nucleotide Polymorphism (SNP) in the lysyl oxidase-like 1 (LOXL1) gene, located on chromosome 15 [2]. The disease is characterised by the abnormal production and progressive accumulation of extracellular, fibrillar, amyloid-like material in various tissues, especially in the eye [3]. These deposits are commonly found on the pupillary margin, anterior lens capsule, zonules, ciliary body, trabecular meshwork, and corneal endothelium [3,4]. The material may also accumulate systemically in organs such as the brain, liver, lungs, and heart, suggesting widespread connective tissue dysfunction [4].

PEX is a global phenomenon, with a prevalence rate of 10 to 20% in the general population aged 60 years and older [5]. Several hospital-based studies in India have reported a prevalence ranging from 1.85 to 13.5% in individuals over 45 [6,7]. PEX is the most frequently reported cause of secondary open-angle glaucoma, accounting for approximately 25-30% of global cases [8]. PXG is typically more aggressive than POAG, as evidenced by higher IOP, greater pressure fluctuations, and faster progression of visual field loss [9]. PXG is also associated with a poorer visual prognosis and reduced responsiveness to conventional therapies [10]. Beyond glaucoma, PEX is linked to several ocular complications, including zonular weakness, poor pupillary dilation, corneal endothelial dysfunction, and increased intraoperative risk during cataract surgery [11].

The CCT is a key parameter in ocular assessment for PEX patients [12]. In healthy individuals, the average CCT is around 540-550  $\mu\text{m}$  [13]. Goldmann Application Tonometry (GAT), the gold standard for IOP measurement, assumes a normal corneal thickness; deviations from this value can significantly affect measurement accuracy [12]. Thinner corneas may result in underestimated IOP readings, while thicker corneas may lead to overestimation [14]. IOP can vary by approximately 0.5-0.7 mmHg for every 10  $\mu\text{m}$  deviation from the average CCT [13].

However, current literature offers conflicting findings regarding CCT in PEX patients. While some studies report no significant differences in CCT between PEX patients and individuals with normal eyes, others suggest that the corneas of affected individuals are either thinner or thicker [15-18]. Additionally, corneal curvature- which influences corneal biomechanics and IOP readings- has not been thoroughly investigated in Indian population. This inconsistency and lack of comprehensive data hinder accurate glaucoma diagnosis and optimal management in PEX patients.

Given these limitations, the present study aimed to assess CCT and corneal curvature in individuals with PEX and compare these parameters with those without PEX. Specifically, the objectives are two fold: 1) to evaluate and compare CCT and corneal curvature between individuals with and without PXF; and (2) to compare these parameters between affected and unaffected eyes in individuals with unilateral PXF. Through this evaluation, the study seeks to enhance understanding of corneal structural changes in PEX. Accurate assessment of corneal parameters will contribute to improved IOP interpretation, earlier glaucoma detection, and more informed clinical

decision-making-ultimately supporting better patient outcomes in this complex condition.

## MATERIALS AND METHODS

The present hospital-based, cross-sectional, study was conducted in the Department of Ophthalmology, Shri BM Patil Medical College, Hospital and Research Centre, Vijayapura, Karnataka, India, between May 2023 and December 2024. The study protocol was reviewed and approved by the Institutional Ethics Committee of Shri BM Patil Medical College, Hospital and Research Centre, Vijayapura, Karnataka, India, under reference number BLDE (DU)/IEC/864/2022-23. All procedures were conducted following the principles of the Declaration of Helsinki.

**Sample size calculation:** The sample size was calculated using G\*Power version 3.1.9.4 software. Based on the study by Ksheeraja Y and Ramya M (2021), the mean CCT was  $561 \pm 25 \mu\text{m}$  in controls and  $536 \pm 24 \mu\text{m}$  in patients with PXF, indicating a significant difference [6]. Cohen's d was calculated based on expected differences in CCT between patients with PXF and healthy controls to approximate the effect size. A mean CCT of  $45.2 \mu\text{m}$  ( $SD=1.8$ ) was assumed for the PXF group and  $43.7 \mu\text{m}$  ( $SD=2.0$ ) for the control group, yielding an estimated effect size (Cohen's d) of approximately 0.8, which corresponds to a significant effect. These values were based on previously published studies that reported comparable differences in CCT between PXF and control populations. Using these parameters, a total sample size of 106 (53 participants per group) was calculated to achieve 98% power at a significance level of  $\alpha=0.05$ . Accordingly, 53 PXF cases and 53 matched controls were ultimately enrolled.

**Inclusion and Exclusion criteria:** A total of 106 eyes from 106 participants were divided into two groups: 53 with clinically diagnosed unilateral or bilateral PXF (PXF group) and 53 control from individuals without signs of PXF or pre-existing corneal pathology. Inclusion in the PXF group was based on the clinical identification of characteristic white fibrillary material on the anterior lens capsule, pupillary margin, or zonules under slit-lamp biomicroscopy [5]. Controls were age-matched individuals attending the Ophthalmology Outpatient Department with no evidence of PXF. Exclusion criteria for both groups included any history of ocular trauma, corneal pathology (e.g., keratoconus or corneal ulcers), previous ocular surgery, or systemic conditions affecting the cornea.

**Data collection procedures:** After obtaining informed consent, participants underwent a comprehensive ocular examination. Visual acuity was assessed using the Snellen chart, and IOP was measured using both a non-contact tonometer and a Schiotz tonometer. The diagnosis of PXF was confirmed by slit-lamp biomicroscopy. CCT was measured using AS-OCT and verified with pachymetry. Corneal curvature was assessed using an autorefractometer, with keratometric readings recorded as K1 (flat meridian) and K2 (steep meridian) for both right (OD) and left (OS) eyes. Fundus examination, including Cup-To-Disc Ratio (CDR) measurement, was performed using indirect ophthalmoscopy and slit-lamp biomicroscopy with a 90D lens. Within the PXF group, eyes affected by PXF were further compared with fellow eyes in unilateral cases, allowing for intra-individual analysis of corneal parameters. Pupil size was recorded for each participant in both eyes using slit-lamp biomicroscopy under standardized lighting conditions and categorised into 2 mm, 3 mm and 4 mm groups. These measurements were then used to compare the distribution of pupil sizes between PXF cases and controls.

## STATISTICAL ANALYSIS

All data were entered into Microsoft Excel and analysed using Statistical Package of Social Sciences (SPSS) version 20. Descriptive statistics were calculated for all variables, including means, standard

deviations, frequencies, and percentages. The independent samples t-test was used to compare continuous variables between the PXF and control groups. In unilateral PXF cases, the paired samples t-test was used for intra-subject comparisons. Categorical variables such as gender, lifestyle factors, and systemic diseases were analysed using the Chi-square or Fisher's-exact test, as appropriate. A p-value  $<0.05$  was considered statistically significant.

## RESULTS

The mean age was similar between cases ( $64.19 \pm 10.15$  years) and controls ( $61.73 \pm 9.16$  years;  $p=0.649$ ). Gender distribution also showed no significant difference ( $p=0.277$ ), with males accounting for 28 (51.9%) of cases and 33 (62.3%) of controls. The prevalence of diabetes was low and comparable in both groups ( $p=0.460$ ). Smoking (38.9 vs. 22.6%) and alcohol use (40.7 vs. 24.5%) were more common among cases than controls, although these differences were not statistically significant ( $p=0.069$  and  $p=0.074$ , respectively) [Table/Fig-1].

Variables	Case (N=53)	Control (N=53)	Chi-square test	p-value
Age in years (Mean $\pm$ SD)	$64.19 \pm 10.15$	$61.73 \pm 9.16$	2.472	0.649
<b>Gender</b>				
Male	28 (51.9%)	33 (62.3%)	1.18	0.277
Female	25 (48.1%)	20 (37.7%)		
<b>Diabetes</b>				
Yes	3 (5.6%)	5 (9.4%)	0.58	0.46
No	50 (94.4%)	48 (90.6%)		
<b>Smoking</b>				
Yes	21 (38.9%)	12 (22.6%)	3.31	0.069
No	32 (61.1%)	41 (77.4%)		
<b>Alcohol status</b>				
Yes	22 (41.5%)	13 (24.5%)	3.19	0.074
No	31 (58.4%)	40 (75.5%)		

**[Table/Fig-1]:** Comparison of demographic and clinical characteristics of case and controls.

Corneal curvature was significantly flatter in PXF cases than in controls in both eyes. In the right eye, the mean K1 and K2 values were lower in cases ( $44.2 \pm 2.0$  D and  $46.1 \pm 1.3$  D) than in controls ( $45.11 \pm 2.03$  D and  $46.9 \pm 1.2$  D), with p-values of 0.024 and 0.005, respectively. Similar differences were noted in the left eye for K1 ( $p=0.002$ ) and K2 ( $p=0.009$ ), indicating significantly steeper corneas in the control group [Table/Fig-2]. Corneal curvature was significantly flatter in PXF cases than in controls in both eyes. In the right eye, the mean K1 and K2 values were lower in cases ( $44.2 \pm 2.0$  D and  $46.1 \pm 1.3$  D) than in controls ( $45.11 \pm 2.03$  D and  $46.9 \pm 1.2$  D), with p-values of 0.024 and 0.005, respectively. Similar differences were noted in the left eye for K1 ( $p=0.002$ ) and K2 ( $p=0.009$ ), indicating significantly steeper corneas in the control group [Table/Fig-2]. The CCT was comparable between cases and controls across both OCT and pachymetry measurements. No significant differences were observed in either eye by either method ( $p>0.6$  for all comparisons), indicating similar corneal thickness in both groups [Table/Fig-3].

Parameters	Case (N=53)	Controls (N= 53)	p-value
K1 (OD) (D)	$44.2 \pm 2.0$	$45.11 \pm 2.03$	0.024*
K2 (OD) (D)	$46.1 \pm 1.3$	$46.9 \pm 1.2$	0.005*
K1 (OS) (D)	$44.06 \pm 1.7$	$45.04 \pm 1.5$	0.002*
K2 (OS) (D)	$46.5 \pm 1.2$	$47.2 \pm 1.3$	0.0009*

**[Table/Fig-2]:** Comparison of K1 and K2 in patients with andwithout Pseudoexfoliation (PXF).

\*shows significant p-value;

A p-value less than 0.05 was considered significant

Variables	Case (N=53)	Controls (N= 53)	p-value
<b>Optical Coherence Tomography (OCT)</b>			
CCT OD (μm)	506.15±36	501.4±34.7	0.626
CCT OS (μm)	503.35±34	504.4±26.40	0.617
<b>Pachymetry</b>			
CCT OD (μm)	506.33±34.3	504.81±32.7	0.621
CCT OS (μm)	505.1±33.2	507.6±25.67	0.612

**[Table/Fig-3]:** Comparison of CCT in patients with and without pseudoexfoliation (PXF) using Optical Coherence Tomography (OCT) and pachymetry.

IOP was significantly higher in the right eye of PXF cases ( $13.6 \pm 1.82$  mmHg) compared to controls ( $12.9 \pm 1.91$  mmHg;  $p=0.011$ ). No significant difference was noted in the left eye ( $p=0.406$ ) [Table/Fig-4]. Among the 14 patients with unilateral PXF, no significant differences were found between the affected and fellow eyes in keratometry, CCT measured by OCT or pachymetry, or IOP ( $p>0.5$  for all comparisons), indicating comparable ocular parameters between the two eyes [Table/Fig-5]. Pupil size distribution was similar between PXF cases and controls in both eyes, with no statistically significant differences observed ( $p=0.834$  for the right eye,  $p=0.714$  for the left eye) [Table/Fig-6].

Parameters	Case (N=53)	Control (N=53)	p-value
IOP OD	$13.6 \pm 1.82$	$12.9 \pm 1.91$	0.011*
IOP OS	$14.12 \pm 1.98$	$13.82 \pm 2.01$	0.406

**[Table/Fig-4]:** Comparison of IOP in patients with and without Pseudoexfoliation (PXF).

\*Shows significant p-value; A p-value less than 0.05 was considered significant

Parameters	Affected eye	Non-affected eye	p-value
<b>K (D)</b>			
K1	$44.9 \pm 2.25$	$44.46 \pm 1.31$	0.633 (NS)
K2	$45.9 \pm 2.28$	$45.7 \pm 2.05$	0.86 (NS)
<b>CCT (μm)</b>			
Optical Coherence Tomography (OCT)	$531.20 \pm 37.6$	$513.7 \pm 50.5$	0.52 (NS)
Pachymetry	$527.8 \pm 36.46$	$513.1 \pm 49.5$	0.58 (NS)
<b>IOP</b>			
	$14.20 \pm 0.44$	$14.13 \pm 2.28$	0.94 (NS)

**[Table/Fig-5]:** Comparison of K1, K2, CCT and IOP in patients with unilateral PXF (N=14).

NS: Not significant p-value

Pupil size (mm)	PXF cases (n=53)	Controls (n=53)	Total (n=106)	Chi-square Test ( $\chi^2$ )	p-value
<b>OD (right eye)</b>					
2 mm	2 (3.7%)	1 (1.9%)	3 (2.8%)	0.363	0.834 (NS)
3 mm	27 (50.9%)	27 (50.9%)	54 (50.9%)		
4 mm	24 (44.4%)	25 (47.2%)	49 (45.8%)		
<b>OS (left eye)</b>					
2 mm	2 (3.7%)	1 (1.9%)	3 (2.8%)	0.673	0.714 (NS)
3 mm	30 (55.6%)	27 (50.9%)	57 (53.3%)		
4 mm	21 (39.6%)	25 (47.2%)	46 (43.3%)		

**[Table/Fig-6]:** Pupil size in cases and controls.

NS: No significant p-value

Patients with PXF had significantly worse visual acuity and more pronounced glaucomatous changes compared to controls. The mean Best-Corrected Visual Acuity (BCVA) was significantly lower in PXF cases (OD: 0.48, OS: 0.44 logMAR) than in controls (OD: 0.30, OS: 0.28 logMAR;  $p<0.05$ ). The average CDR was also significantly higher in PXF eyes (OD: 0.52, OS: 0.51) compared to controls (OD: 0.43, OS: 0.44;  $p<0.05$ ). A significantly greater proportion of PXF eyes had CDR  $\geq 0.6$  {11 (20.8%) vs. 11 (5.6%)}

$p=0.019$ } and glaucomatous optic disc changes (17% vs. 0%;  $p=0.003$ ) [Table/Fig-7].

Parameters	PXF Cases (n=53)	Controls (n=53)	p-value
BCVA OD (logMAR)	0.48±0.22	0.30±0.18	0.032*
BCVA OS (logMAR)	0.44±0.20	0.28±0.16	0.029*
BCVA OD (Snellen equiv.)	6/18	6/12	0.032*
BCVA OS (Snellen equiv.)	6/15	6/12	0.029*
CDR OD (Mean±SD)	0.52±0.12	0.43±0.09	0.011*
CDR OS (Mean±SD)	0.51±0.11	0.44±0.08	0.016*
Eyes with CDR $\geq 0.6$	11 (20.8%)	3 (5.6%)	0.019*
Disc changes suggestive of glaucoma	9 (17%)	0 (0%)	0.003*

**[Table/Fig-7]:** Comparison of Visual acuity and cup to disc ratio in PXF and control group.

\*Shows significant p-value; p-value less than 0.05 was considered significant; BCVA: Best corrected visual acuity

## DISCUSSION

Compared to healthy controls, the present study evaluated CCT, corneal curvature, and various demographic and lifestyle parameters in patients with PXF. The age distribution revealed that most participants were between 60 and 69-year-old, aligning with findings by Forsman E et al., and confirming that PXF primarily affects older individuals [19]. Although a female predominance has been reported in previous literature [20,21], this study observed a higher proportion of males, consistent with findings by Pavicic-Astalos J et al., [22]. However, neither age nor gender showed statistically significant differences, suggesting that these may not serve as independent risk factors across all populations.

Diabetes mellitus was slightly less prevalent in the PXF group, though the difference was insignificant. While some studies [23,24] have linked diabetes to PXF through mechanisms such as oxidative stress and microvascular dysfunction, others, including Detorakis ET et al., , have not established a strong association [25]. Current findings contribute to this uncertainty and indicate that larger multicenter studies are needed to explore potential metabolic associations more conclusively.

Regarding lifestyle factors, smoking and alcohol consumption were more frequently reported among PXF patients, with p-values approaching statistical significance. Although inconclusive, these trends suggest that such exposures may contribute to PXF pathophysiology via oxidative stress mechanisms, supporting the hypothesis proposed by Thorleifsson G et al., [26]. These associations merit further investigation with larger sample sizes.

Keratometry values (K1 and K2) were significantly lower in PXF patients, indicating flatter corneas than controls. This contrasts with studies such as Hepsen IF et al., which reported steeper corneal curvatures in PXF eyes [18]. The flattening observed in the present study may result from biomechanical changes due to the accumulation of pseudoexfoliative material. Clinically, flatter corneas may lead to underestimation of IOP when measured by Goldmann Applanation Tonometry (GAT). Yazgan S et al., highlighted this concern. They recommended alternative tonometry methods, such as Dynamic Contour Tonometry (DCT) or the Ocular Response Analyser (ORA), to avoid IOP measurement errors in PXF patients [27].

The CCT measurements obtained via OCT did not differ significantly between PXF cases and controls, contradicting studies such as those by Zare MA et al., and Tomaszewski TB et al., which reported notable corneal thinning in PXF eyes [28,29]. These discrepancies may be due to differences in study populations, disease severity, or measurement techniques. Nonetheless, in current study absence of significant CCT thinning suggests that corneal thickness changes in PXF may be variable and not universal. Given that a 10 μm reduction in CCT may lead to a 0.5 mmHg underestimation of IOP

[13], clinicians should continue to interpret IOP values cautiously in PXF patients.

Similarly, pachymetry-based CCT measurements showed no significant differences between PXF and control groups, reinforcing the OCT findings. This may indicate that CCT is preserved during the early or moderate stages of PXF. Palko JR et al., reported that significant thinning may only be evident in more advanced glaucomatous PXF cases [17]. In present study, including both glaucomatous and non-glaucomatous PXF eyes may have obscured such stage-dependent differences.

The IOP was significantly higher in the right eyes of PXF patients than controls, a finding that contradicts the results of Boshra MN et al., who found no significant differences [30]. This discrepancy may reflect differences in study design or population characteristics and highlights the need for standardised IOP measurement and subgroup analysis by disease severity.

In the subgroup, analysis of unilateral PXF patients, no significant differences were observed between affected and fellow eyes regarding K1, K2, or CCT measured by either OCT or pachymetry. While Hepsen IF et al., found elevated keratometric values in PXF eyes, meanwhile the subgroup of present study was limited by a small sample size (n=14), which reduced the statistical power to draw definitive conclusions [18]. Nonetheless, the results suggest that unilateral PXF may not be associated with significant corneal changes in the early phase of the disease.

Pupil size measurements did not differ significantly between PXF and control groups which was consistent with mixed findings in the literature. Some researchers, such as Wishart PK and Spaeth GL have reported smaller pupil sizes in PXF due to iris sphincter dysfunction or pigment dispersion [31]. In contrast, current findings revealed similar pupil size distributions across both groups, suggesting that pupillary changes may not be apparent in the early or moderate stages of the disease. More detailed evaluation using dynamic pupillometry may help detect subtle functional alterations.

### Limitation(s)

Despite its strengths, this study has several limitations that warrant consideration. The study was conducted at a single tertiary care center, potentially introducing referral bias and limiting the applicability of the results to broader community settings. Multicenter studies involving diverse geographic and ethnic populations must validate and expand upon these findings. Although AS-OCT and pachymetry were used to measure CCT, corneal biomechanics- such as corneal hysteresis and corneal resistance factor- were not assessed. These parameters could offer deeper insights into the structural integrity and vulnerability of the cornea in PXF patients. The cross-sectional design limits the ability to draw causal inferences or evaluate the progression of corneal changes over time. A longitudinal follow-up would better capture disease progression and the potential impact of PXF on corneal parameters and glaucoma development. Lastly, IOP measurements were not performed using GAT the clinical gold standard but instead employed non-contact and Schiotz tonometers. The influence of corneal properties on IOP readings may have affected the accuracy of pressure estimation, particularly in eyes with altered curvature or CCT.

### CONCLUSION(S)

The present study demonstrates that patients with PXF have significantly lower K1 and K2 values than controls, indicating flatter corneas. Flatter corneas may lead to an underestimation of IOP. Early recognition of corneal flattening in PXF patients can aid in better risk assessment and management of glaucoma. The present study observed no significant difference in CCT between the case and control groups. CCT was measured using advanced imaging modalities such as AS-OCT. Integrating these findings into routine

ophthalmic practice may enhance diagnostic precision and improve patient outcomes in PXF-related ocular disorders.

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