“EVALUATION OF DIURNAL VARIATION OF INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS IN PSEUDOEXFOLIATION EYES”

By

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Dissertation submitted to

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In partial fulfilment of the requirements for the degree of

MASTER OF SURGERY

IN

OPHTHALMOLOGY

Under the guidance of

DR.INCHARA N M.B.B.S., M.S.

DEPARTMENT OF OPHTHALMOLOGY

SRI DEVARAJ URS MEDICAL COLLEGE

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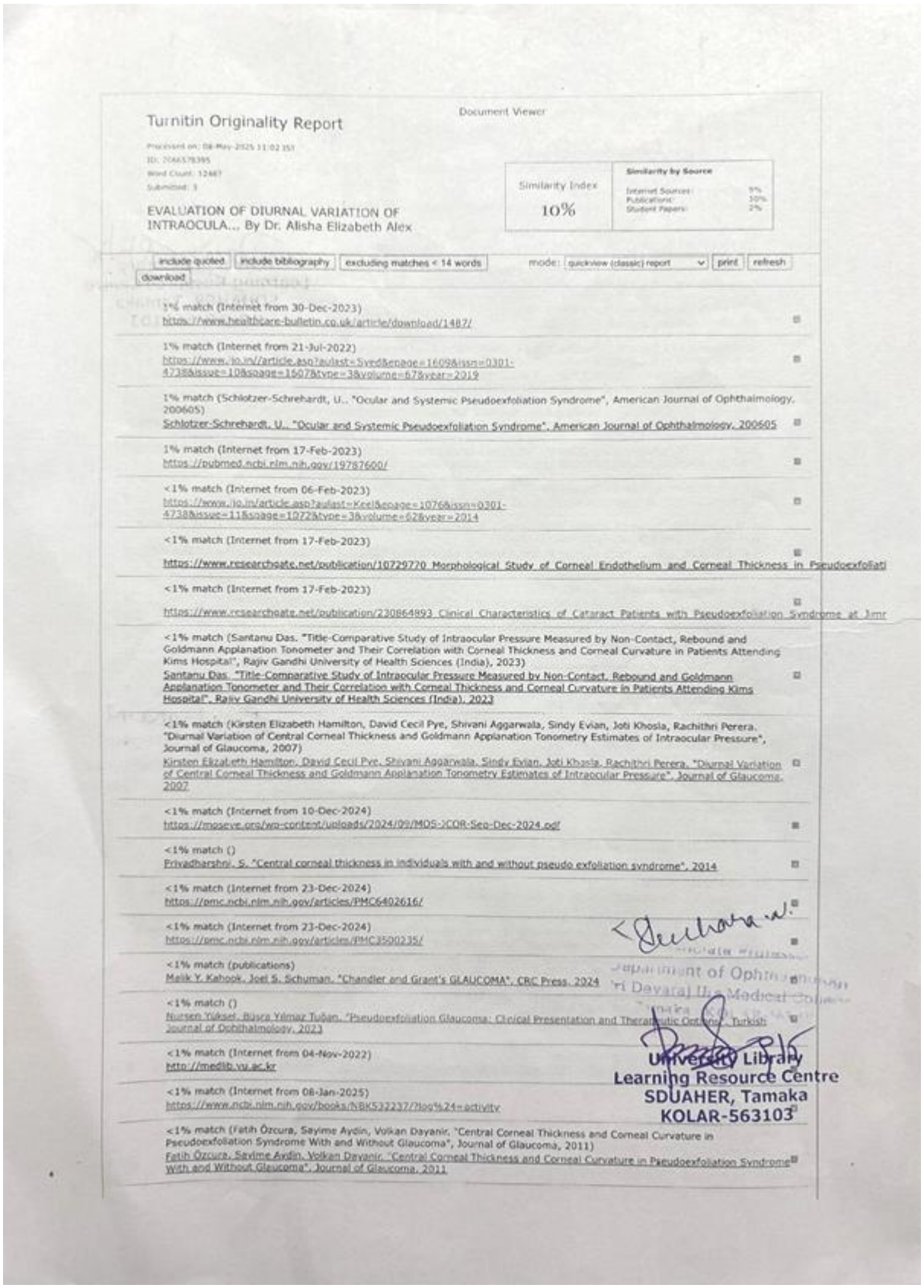

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LIST OF ABBREVIATIONS

IOP	**Intraocular pressure**
PXS	**Pseudoexfoliation Syndrome**
PXF	**Pseudoexfoliation**
PXM	**Pseudoexfoliation material**
TIA	**Transient Ischemic Attack**
LOXL-1	**Lysyl Oxidate-Like 1**
ECM	**Extracellular Matrix**
SNP	**Single Nucleotide Polymorphism**
TGF-β1	**Transforming Growth Factor-Beta-1**
CCT	**Central corneal thickness**
GAT	**Goldmann Applanation Tonometry**
OCT	**Optical Coherence Tomography**
AH	**Aqueous Humor**
CNTNAP2	**Contactin-Associated Protein-Like 2**
POAG	**Primary open angle glaucoma**
PXFG	**Pseudoexfoliative glaucoma**
SLT	**Selective Laser Trabeculoplasty**

ABSTRACT

Background: Pseudoexfoliation syndrome (PXS) is an age-related systemic disorder characterized by an accumulation of abnormal white flaky substances on the anterior segment of the eyeball. Large diurnal IOP fluctuations were reported to be an independent risk factor for the progression of glaucoma. The recognition of a diurnal variation is important for diagnostic and therapeutic reasons. The present study was done to measure and correlate the diurnal variation in the central corneal thickness and intraocular pressure in Pseudoexfoliation eyes

Methods: A prospective observational study was conducted among total of 51 eyes with pseudoexfoliation eyes. All subjects will be assessed by four measurements of intraocular pressure and central corneal thickness during hospital hours on a single day at 4 sessions 8 AM, 11 AM, 2 PM and 5 PM by a single examiner to avoid any bias.

Results: Mean age of the patients in the study was 68.96 years. Most of the patients in the study were males (52.9%). The mean CCT at 8 AM, 11 AM, 2 PM and 5 PM were 524.22, 521.1, 520.37 and 515.51, respectively. The mean IOP at 8 AM, 11 AM, 2 PM and 5 PM were 17.75, 17.55, 17.29 and 16.82, respectively. There was significant negative correlation between CCT and IOP at all time points ($p<0.05$). There was a significant decrease in CCT over the course of time in the day, while no significant variation in the IOP was observed.

Conclusion: A significant decline in central corneal thickness in the diurnal variation assessment among patients with pseudoexfoliation eyes was observed. We concluded that there was a negative correlation between the CCT and IOP at individual time point assessments.

Keywords: Central Corneal Thickness, Intra Ocular Pressure, Pseudoexfoliation , Variation

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INTRODUCTION

EVALUATION OF DIURNAL VARIATION OF INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS IN PSEUDOEXFOLIATION EYES

INTRODUCTION

Pseudoexfoliation syndrome (PXS) is an age-related systemic disorder characterized by an accumulation of abnormal white flaky substances on the anterior segment of the eyeball.[1] Worldwide 60 to 70 million people are estimated to be affected by PXS.[2] The prevalence of disease varied based on geographical location, ethnicity, environment, demography, genetic and molecular risk.[3]

About 15 % to 30% of the population identified as pseudoexfoliation syndrome, subsequently forms into pseudoexfoliation glaucoma.[3] PXS often leads to significant alterations in intraocular pressure (IOP). IOP fluctuations may play a critical role in the onset and progression of glaucomatous optic neuropathy. Diurnal variations in IOP, a recognized phenomenon in normal and diseased eyes, are particularly pronounced in pseudoexfoliation(PXF), underscoring the need for targeted investigations in this population. Understanding these variations is imperative for early diagnosis, risk stratification, and effective management of PXF-related glaucoma.[4,5]

Central corneal thickness (CCT) is another key parameter that influences the accuracy of IOP measurement. Variations in CCT not only affect the reliability of tonometric readings but also serve as an independent risk factor for glaucoma progression. Thinner corneas are associated with an increased risk of glaucomatous damage, while variations in CCT throughout the day can further complicate clinical assessments. In eyes with pseudoexfoliation, structural changes in the cornea,

combined with altered biomechanical properties, may lead to distinct patterns of diurnal variation in CCT. Exploring these patterns is critical for improving the precision of IOP measurements and optimizing glaucoma management in affected individuals.[6,7]

Although diurnal variations in IOP and CCT are well-established phenomena, limited data exist regarding their behaviour in pseudoexfoliation syndrome. The unique pathophysiological changes in PXF, including compromised trabecular meshwork function and increased susceptibility to oxidative stress, are likely to influence these parameters differently compared to non-PXF eyes. By investigating the diurnal profiles of IOP and CCT in this specific context, we can gain valuable insights into the disease mechanisms and their clinical implications.[6,8]

Accurate assessment of diurnal variations in IOP and CCT is crucial for tailoring management strategies for pseudoexfoliation syndrome. Current clinical practices often rely on single-time-point measurements, which may not capture the full extent of fluctuation in these parameters. This limitation could lead to underestimation of glaucoma risk or suboptimal therapeutic interventions. Incorporating a better understanding of diurnal patterns into routine practice may enhance the effectiveness of both diagnostic and therapeutic approaches.[4,9]

Through this investigation, we aim to elucidate the interplay between IOP and CCT variations in pseudoexfoliation eyes, enhancing our understanding of the disease dynamics. This knowledge is anticipated to pave the way for improved monitoring schedules and more effective intervention strategies, ultimately reducing the burden of vision loss associated with PXF-related glaucoma. By addressing the gaps in current understanding, this study aspires to make a meaningful contribution to the

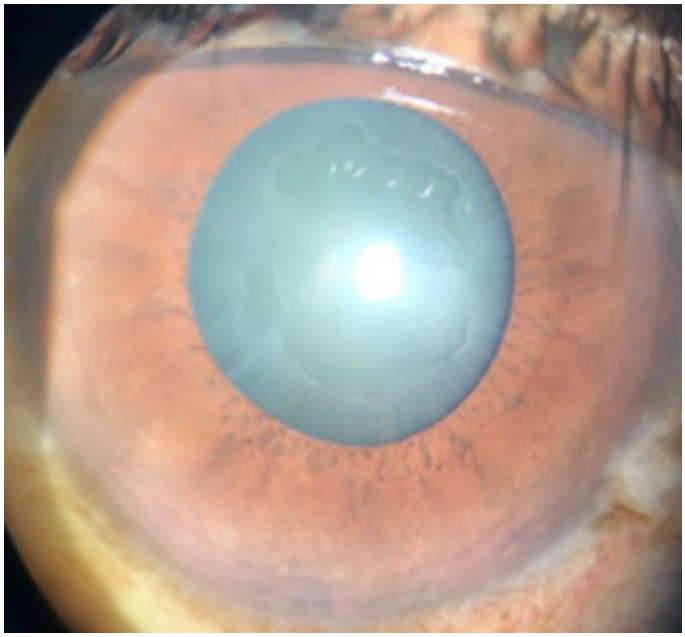
field of ophthalmology and the care of individuals affected by pseudoexfoliation syndrome

Pseudoexfoliation syndrome:

The common sites of PXS are trabecular meshwork, anterior capsule of lens, anterior surface of iris, and cornea.[1] The abnormal regulation of the elastin synthesis process, the production of abnormal elastin fiber aggregates, and the decrease in collagen fibers result in the formation of pseudoexfoliation material. This plays an important role in secondary glaucoma formation called pseudoexfoliation glaucoma, which could cause blindness most of the time.[10,11] It is frequently connected with secondary open-angle glaucoma and cataracts.[5,12] PXS is the common cause of ocular hypertension and glaucoma. PXS also causes non-ocular diseases like coronary artery disease, and recently pelvic organ prolapse.[13]

Pseudoexfoliation material (PXM) is a distinctive fibrillar extracellular material. These fibrils are composed of 8 to 10 mm diameter of microfibrils. The fibrils are coated with electron-dense amorphous materials.[14] These are produced and secreted by epithelial cells, fibroblasts, and smooth muscle cells of different ocular and systemic tissues. This PXM is composed of protein components like fibrillin-1, elastin, collagens, emilin, laminin, and fibronectin. Glycosaminoglycans like hyaluronic acid, chondroitin sulfate, and heparan form the fibrillar structure. Other components involved are amyloid-like material, oxidative stress markers, and matrix metalloproteinases and their inhibitors.[5,15,16]

Figure 1: Deposition of PEX material on Anterior lens capsule.[17]



Epidemiology:[18]

Over the age of 60, the global prevalence rate is 10-20%. Under the age of 60, the prevalence is 0.5%.[19] This occurs almost in all geographical regions.[5] From different parts of the world, the PXS prevalence varies from 0% to 38%.[20] The prevalence of PXS is 0.3% in Mongolia and 18% in Sweden. The prevalence of PXS was higher in European populations. They found the prevalence of Icelanders, Finns, Russians, and Lapps as 21%. In contrast, England has 4.7%, Germany has 4% and Norway has 6% of prevalence. In India, the prevalence rate above the age of 45 was 1.8% to 13.5%.[21,22] In South India, the prevalence is between 3.8% and 6%, among patients 40 years and older. In Central India, the prevalence is 3.5% in people above 30 years. The highest prevalence of about 41%, between the age group of 61 to 70, and about 29% between the age group of 71 and 80 was seen in states of India like Telangana, Karnataka, Andra Pradesh, and Orissa.[23] In Pakistan, they reported a prevalence of 6.45%.[24] In Singapore, they reported a prevalence of 2.8%.[25] About

48% to 76% of PXS patients were affected by unilateral PXS, which developed into bilateral PXS in 50%, within 5 to 10 years.[21] The incidence of PXS, between the age group of 70 and 74 years was 14%, 75 and 79 years was 28%, 80 and 84 was 26%, and above 80 years was 30%. Some studies show that both sexes are equally affected by PXS, while in some studies women are more prone to PXS than men. This may be because women have longer lifespans and older age is the risk factor. [2,10,26]

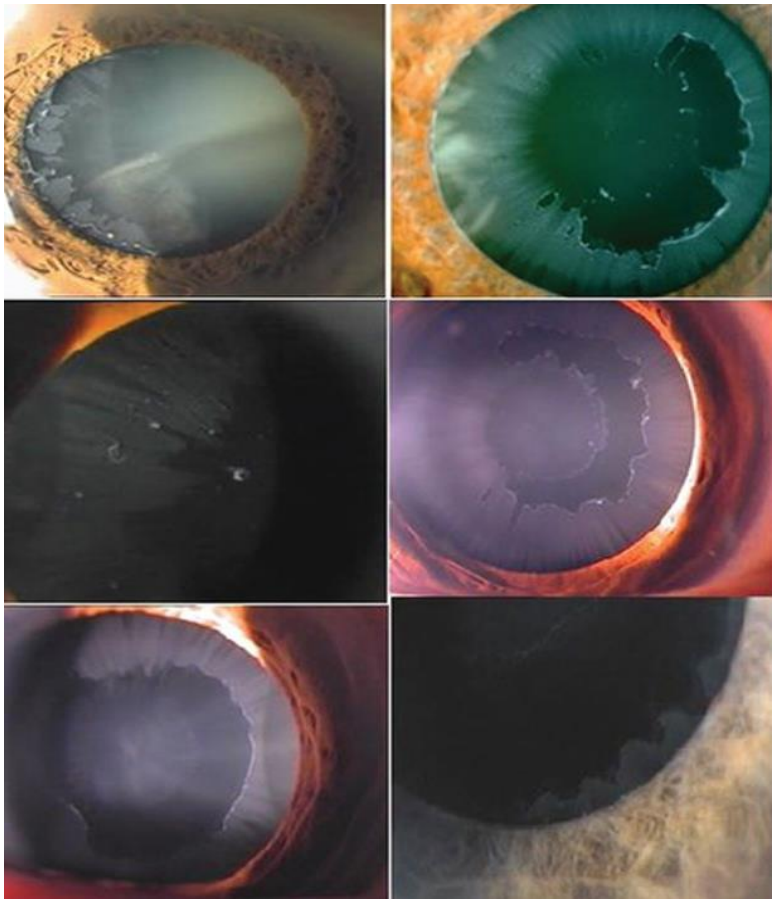
Risk factors:

Older age is the major risk factor, mostly over 60. The people near the Nordic and eastern Mediterranean have a higher risk. Environmental risk factors like long duration of sunny days, UV exposure, cosmic radiation, higher altitude, and outdoor work cause PXS.[11,27,28] Dietary factors like high intake of dietary products, consumption of coffee for long periods, and folate deficiency, cause PXS.[29] High and prolonged consumption of alcohol and cigarette usage also leads to PXS.[5,10] PXS is also correlated with cardiovascular diseases, hypertension, TIA, aneurysms, thromboses, cerebral ischemia, and sensorineural hearing loss. A significant correlation was also found between PXS and cardiovascular diseases.[3,30] As PXS eyes have poor dilatation and lens zonule instability, this forms a higher risk of capsular bag rupture, and loss of vitreous and zonular dialysis. Another important risk factor is oxidative stress. [2,11,16] This is often combined with open-angle glaucoma, poor pupillary dilatation, and melanin dispersion and sometimes it is present along with keratopathy.[31,32] Vitamin deficiencies are also associated with PXS. The PXS results in significant mortality and morbidity and without cure. Thus, PXS is concluded as a public concern.[3]

Pathogenesis:

The abnormal extracellular fibrillar materials production and deposition leads to PXS, which is produced by cells of the trabecular meshwork, iris, ciliary body, and lens epithelium and deposited on the anterior wall of the eyes. The excess production of elastic microfibril and also its insufficiency plays a role in this condition.[5] Increased oxidative damage may contribute to the pathogenesis of PXS. An increase in IOP in PXS leads to glaucoma development.[5] Progressive damage or degenerative changes to Schlemm's canal and juxtacanalicular tissue increase the IOP. The role of systemic involvements like pseudoexfoliation material accumulation in extraocular tissues, like valves of the heart, skin, and blood vessels is also associated.[15]

Figure 2: Pseudoexfoliation deposition on the anterior surface of the lens.[2]



The four factors included in PXS pathogenesis are miRNA expression alteration, disordered autophagy, mitochondrial mutation involvement, and compromised aqueous-blood barriers.[11] The polymorphism of the lysyl oxidate-like 1 (LOXL-1) enzyme and CACNA1A locus are the primary genetic risk factors in PXS formation. The LOXL-1 gene encodes an enzyme that is crucial for elastic fiber formation and maintenance in connective tissues. Their dysfunction can lead to the accumulation of pseudoexfoliation material, causing PXS. The LOXL-1 has the function of cross-linking the elastin and collagen inside the extracellular matrix (ECM), hence it plays an important role in PXS development. The three single nucleotide polymorphisms (SNPs) of LOXL1 are rs1048661, rs3825942, and rs2165241, the crucial risk factors. These variants change the LOXL-1 function and damage the homeostasis of elastic fiber resulting in the deposition of materials.[33–35] Thus, they concluded that the genetic variants of LOXL-1 affect the elastin-related gene regulation and ECM, contributing to PXS formation. Additionally, SEMA6A, AGPAT1, FLT1-POMP, TMEM136-ARHGEF12, and RBMS3 were also associated.[3,10,29] The Chromosome 8p21, clusterin gene, Chromosome 1p13.3, Glutathione transferase, and Fibrulin-5 gene also lead to abnormal fibrillar material accumulation in the eyes. Transforming growth factor-beta-1 (TGF-β1) is responsible for the development of the abnormal accumulation. This increases the pseudoexfoliation material production in vitro, thus increasing the concentration of aqueous humor of PXS eyes. Hypoxia in the anterior chamber and iris hypoperfusion also cause PXS.[11,36]

Figure 3: Deposition of pseudoexfoliation material on corneal endothelial surface in pseudoexfoliation syndrome.[2]

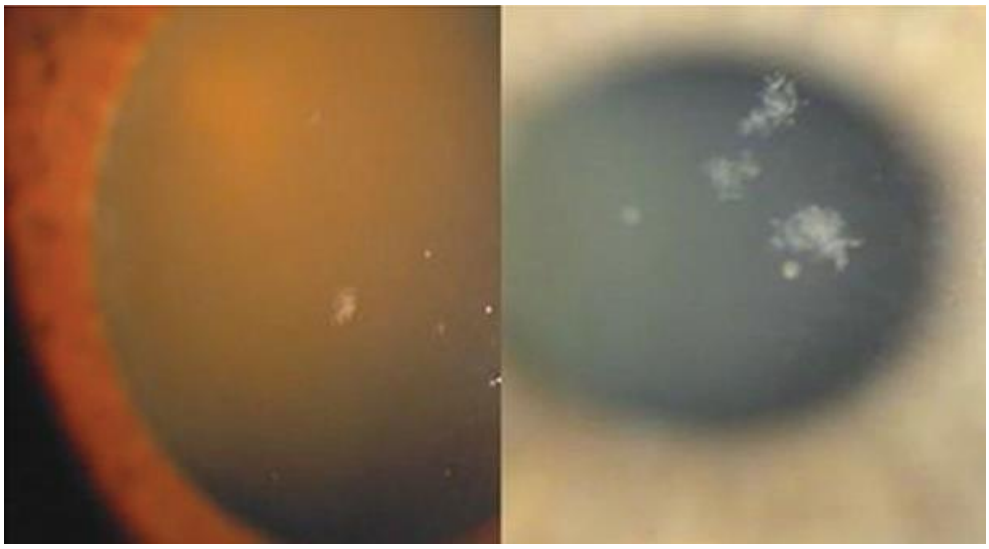


Figure 4: White flake deposit and "moth-eaten" pattern on the pupillary margin.[2]

Clinical manifestations:[2,9,37]

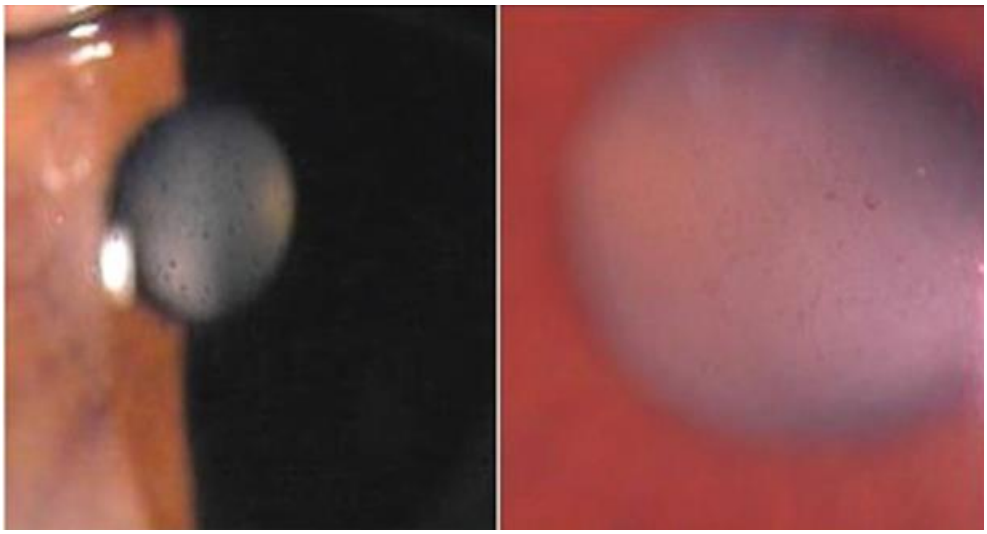
- Primary risk factor for glaucoma: PXS is the major risk factor for pseudoexfoliation glaucoma, causing IOP elevation and damage to the optic nerve.

- Glaucoma progression: PEX patients are more likely to develop glaucoma, compared to non-PXS people. Due to obstruction of trabecular meshwork, secondary open-angle glaucoma is formed.[9]
- Prevalence: PXS increases with older age and geographical changes and environment.
- Systemic association: PXS is associated with cardiovascular and Alzheimer's diseases.
- Surgical complications: PXS have a higher risk during cataract surgery, like instability of zonules and rupture of the capsule.
- Impact on corneal endothelium: PXS is linked with dysfunction of the corneal endothelium, which affects the transparency of the cornea and causes abnormalities.
- Impact on lens pathology: Accumulation of PXM leads to phacodonesis and causes dislocation of the lens.
- Impact on retinal vein occlusion: Due to alterations of vascular structures, PXS may higher the risk of occlusion of retinal veins.
- This includes ocular signs such as a change in iris or sphincter transillumination, zonular weakness, pigment dispersion on the iris and trabecular meshwork, pupillary ruff defects, and exfoliation material on the ciliary body and zonules.
- The breakdown of the blood-aqueous barrier in a prolonger manner causes secondary cataracts in PXS eyes.[31]
- In recent studies, the PXS is associated with an increase in carotid intima-media thickness and an increase in retinal artery resistance.[38]

Diagnosis:[2,9,11]

1. Noticing pseudoexfoliation material on PXS eyes regularly, with dilated pupils helps in diagnosing PXS.[5]
2. Slit-lamp biomicroscopy uses a narrow-slit beam to evaluate the anterior segment of the eye from left to right to examine fibrillar accumulation over the lens capsule and pupillary margins. The slit-lamp photos are captured by photo-slit-lamp cameras. The density of deposited material was graded on a 3-level scale. The pigment deposition on the corneal endothelium and trabecular meshwork can also be detected.[5,39]
3. High-resolution ultrasound biomicroscopy detects the deposited materials on zonules and lenses early. Assess the lens position and zonular integrity.
4. Gonioscopy detects the angle structures pigment and PXM deposition in the trabecular meshwork. This is performed along with a slit-lamp examination.[5,11]
5. Optical coherence tomography in early diagnosis of glaucomatous damages by evaluating alterations in optic nerve head and retinal nerve fiber layers.
6. Specular microscopy measures the corneal endothelial damage and decreased cell density, especially in cataract surgery undergoing PXS patients.
7. Optic disc alterations and thinning of the retinal nerve fiber layer should be assessed. The visual field should be tested for functional loss.

Figure 5: Pigmentary deposition on the surface of corneal endothelium in pseudoexfoliation eyes.[2]



Central corneal thickness (CCT):[40]

It is a measurement of the thickness of the central portion of the cornea. The CCT affects the values of intra-ocular pressure. It is measured in micrometres (µm). The normal CCT ranges between 520 to 580 µm. The CCT < 520µm is considered a thin cornea and CCT > 580 µm is considered a thick cornea. However, CCT also varies according to age, gender, IOP, genetics, and other factors. The average CCT in the age group between 18 and 29 is 550.8µm, between 30 and 39 is 557.5µm, between 50 and 59 is 551.3µm, between 60 and 79 is 544.2µm, between 70 and 79 is 535.1µm and between 80 and 89 is 530.1µm.[41] The thicker corneas have higher values and thinner corneas have lesser values. CCT is crucial for accurate IOP measurement, a primary diagnostic criterion for glaucoma.

Table 1: Methods of measurements:[30,40,42,43]

S.No	Method of Measurements	Contact/ non-contact with eyes	What It Measures
1	Ultrasound Pachymetry	Contact	Corneal thickness via ultrasound waves
2	Optical Coherence Tomography (OCT)	Non-Contact	Corneal thickness using light waves
3	Scheimpflug Imaging (e.g., Pentacam)	Non-Contact	3D reconstruction of cornea and CCT
4	Confocal Microscopy	Contact	Corneal layers and thickness
5	Specular Microscopy	Non-Contact	Endothelial cell counts and CCT
6	Orbscan	Non-Contact	CCT and corneal topography
7	Optical Low-Coherence Reflectometry	Non-Contact	Corneal thickness via light interference
8	Anterior Segment OCT	Non-Contact	High-resolution corneal imaging and CCT
9	Laser Doppler Interferometry	Non-Contact	Corneal thickness via laser interference
10	Ultrasound Biomicroscopy	Contact	CCT and anterior chamber details

Clinical significance:[43–46]

- **Influence on IOP Measurements:** CCT affects the accuracy of IOP values obtained from applanation tonometry. Corneas which are thinner may result in IOP

underestimation and ones which are thicker result in IOP overestimation. This has significant implications for glaucoma diagnosis and management.

- **Glaucoma Risk Assessment:** An identified independent risk factor for the formation and progression of glaucoma is thinner CCT. Patients with decreased CCT should be careful in monitoring to assess the glaucomatous changes.
- **Ethnic Variations:** The CCT varies based on different ethnic groups. For example, as compared to Caucasians African Americans tend to have thinner corneas and this may lead to a higher prevalence and severity of glaucoma in this population.
- The important clinical significance of CCT is diagnosing, risk stratification, deciding what treatment should be performed, post-refractive surgery challenges, monitoring the disease, and follow-up.
- Thinner CCT is associated with a higher risk of diseases and needs aggressive treatment. A lower CCT value (thinner CCT) denotes a higher risk of glaucoma formation.
- In ocular hypertension patients, thinner CCT denotes the risk of developing primary open-angle glaucoma. When CCT is reduced by 40 µm, the risk of primary open-angle glaucoma increases by 1.71.
- It plays an important role in clinical management and in assessing glaucoma, and ocular hypertension and in examining the eligibility of patients for laser refractive surgery.

Intraocular pressure:[47]

Intraocular pressure (IOP) or eye pressure is defined as the fluid pressure of the eye. The continuous fluid production and outflow maintain this pressure. The IOP is a measurement of the magnitude of the force released by aqueous humor (AH) on the

internal surface area of the anterior eye. Between AH production and drainage, the IOP presents as a fine-tuned equilibrium. The IOP is maintained by intricate homeostatic mechanisms. Aqueous production is regulated by the sympathetic nervous system, with alpha-2 receptors decreasing the secretion and beta-2 receptors increasing the secretion.

Goldmann's equation determines the IOP:[47]

- ❖ IOP = (F/C) + P
- F = Aqueous humor flow rate
- C = Aqueous humor outflow
- P = Episcleral venous pressure
- ❖ IOP is measured in millimetres of Mercury (mmHg).
- ❖ The normal IOP value ranges from 10 to 21 mmHg.[48]

Table 2: Methods of measurements:[48–51]

S.No	Methods of Measurement	How it measures
1	Goldmann Applanation Tonometry (GAT)	Measures IOP via corneal flattening
2	Non-contact tonometry (Air-Puff)	Measures IOP via corneal deformation with air
3	Tono-Pen	Portable tonometer that directly measures IOP
4	Perkins Applanation Tonometer	Handheld version of Goldmann tonometry
5	Dynamic Contour Tonometry (Pascal)	IOP measurement independent of corneal properties
6	Pneumatonometry	Measures IOP using a pneumatic system

7	Rebound Tonometry (e.g., iCare)	Measures IOP by detecting motion rebound
8	Schiotz Indentation Tonometry	Measures IOP via corneal indentation
9	Ocular Response Analyzer	Measures IOP and corneal hysteresis
10	Transpalpebral Tonometer	Measures IOP through the eyelid

Figure 6: Goldmann Applanation tonometry positioned on the slit-lamp:[51]

Clinical significance:[47]

- Sudden IOP increase leads to mechanical stress and ischemic damage on retinal nerve fiber layers.
- The dissolved gases in the microvasculature may cause the development of microbubbles in case of a sudden IOP decrease and lead to gas emboli and ischemic damage in tissues.

- ❖ Chronic IOP increase is the key factor in primary open-angle glaucoma (POAG) development and other serious vision problems.
- ❖ Ocular hypertension is identified as IOP greater than 21 mmHg.
- ❖ IOP lesser than 7 mmHg is identified as ocular hypotony.
- ❖ In the measure of the circadian rhythm of IOP, in the morning IOP will be higher and in the evening IOP will be reduced.
- ❖ In pseudoexfoliation syndrome, the accumulation of materials can cause an increase in IOP within the eyes, which could cause glaucoma and various vision problems. The diurnal IOP fluctuation was also greater in PXS eyes than in normal eyes.[2]

IOP and CCT in pseudoexfoliation (PEX):

- ❖ **IOP in pseudoexfoliation:**

- In PXS, the IOP is often higher than the normal range due to compromised AH outflow caused by PXM material accumulation on the trabecular meshwork. This leads to greater resistance to aqueous drainage and subsequent increase in IOP, but it may widely vary.[7]
- In PXS, diurnal changes of IOP were also observed, with increased fluctuation in IOP value and marked pressure spikes. This fluctuation may be attributed to various positions of the body. For example, the anterior chamber depth is decreased and IOP is raised in the prone position. This fluctuation causes optic nerve damage.[8]
- In PXFG, the IOP may exceed up to 30 mmHg if not treated as it markedly increases compared to PXS. This higher elevation of IOP is associated with damage to the optic nerve, and it is rapidly progressed compared to POAG. The PXFG has unstable IOP levels.[5]

❖ **CCT in pseudoexfoliation:**

- The CCT is most commonly decreased in PXS, indicating thinner CCTs. The CCT value in PXS ranges approximately from 520 to 540 µm, which denotes CCT as slightly thinner. The cell abnormality in corneal endothelium and abnormalities in structure due to PXM accumulation leads to thinning of CCT.[52]
- A thinner cornea can lead to underestimation of IOP values when using Goldmann applanation tonometry, potentially delaying the diagnosis and treatment of elevated IOP in PXS patients. Additionally, thinner CCT is considered an independent risk factor for the development and progression of glaucoma.[8]
- The CCT values in PXFG were also reduced. The CCT value in PXFG ranges approximately from 500 to 520 µm, which denotes CCT as significantly thinner.[44,53]

❖ **Correlation between IOP and CCT in pseudoexfoliation:**[4,7,8]

- Thinner corneas can result in underestimation of IOP, potentially not revealing the actual risk of glaucoma formation. Hence, CCT measurement is essential for accurate IOP evaluation and risk stratification in PXS patients.
- In PXS patients, for early diagnosis and treatment of glaucoma understanding the association between CCT and IOP is important. Both parameters should be regularly monitored to aid in timely intervention, and potentially help in preventing and slowing the progression to PXFG.

Complications:[5,9,14]

1. **Clinical complications:**[5,54]

- **Complications of lens, ciliary body and zonules:**

  Cataract, phacodonesis, lens subluxation, zonular instability, lens dislocation, and angle-closure glaucoma due to pupillary and ciliary block.

- **Complications of Iris:**

  Melanin dispersion, poor mydriasis, iris rigidity, capillary haemorrhage, blood-aqueous barrier defects, pseudouveitis, anterior chamber hypoxia, and posterior synechiae.

- **Complications of trabecular meshwork:**

  Intraocular hypertension and open-angle glaucoma (PXS patients have a 2 to 3 times higher risk of POAG).

- **Complications of Cornea:**

  Endothelial decompensation, and endothelial proliferation.

- **Complications of posterior segment:**

  Retinal vein occlusion.

2. **Surgical complication:**[5,54]

- **Complications of the lens, ciliary body, and zonules:**

  Zonular rupture/dialysis, vitreous loss, posterior capsule rupture, decentration of lens implant, anterior capsule fibrosis and secondary cataract.

- **Complications of Iris:**

  Miosis/ poor surgical evaluation, intra- and post-operative hyphema, post-operative inflammation, prolonged blood-aqueous barrier breakdown, posterior synechiae and pupillary block.

- **Complications of trabecular meshwork:**

  Post-operative increase in intra-ocular pressure.

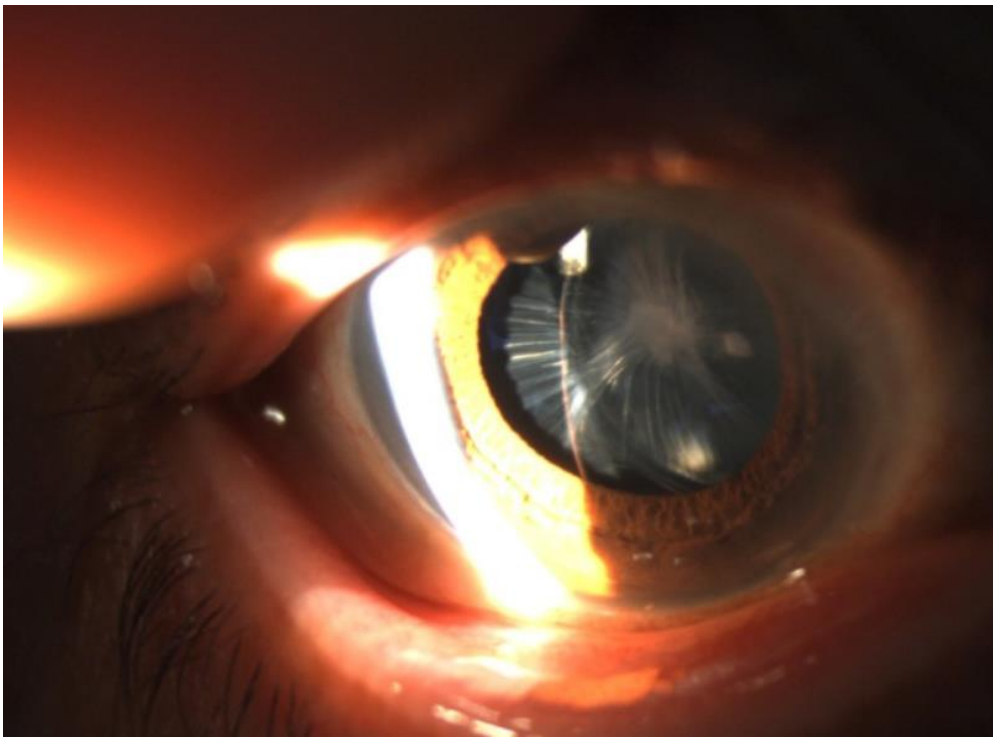
- **Complications of Cornea:**

  Endothelial decompensation.

3. PXFG is a common and aggressive complication.
4. PXM deposition sometimes leads to sensorineural hearing loss.

5. Vascular abnormalities - hypertension, aneurysms, and vascular diseases.
6. Cardiovascular diseases - ischemic heart diseases, stroke, aortic aneurysms

Figure 7: Intra-ocular lens dislocation in PXS patient due to anterior capsule phimosis postoperatively:[54]



PEX Progression into glaucoma:

Secondary glaucoma:

- A study demonstrated that 5% of people with PXS can be affected by PXFG in 5 years, this can be increased to 15% in 10 years and up to 60% in 15 years.[55] The development of secondary glaucoma is cumulative. Also, the important risk factor is IOP.[2] The factors that are involved in PXFG development from PXS are IOP, degree of pupil dilation, and IOP difference between the fellow eyes.[5]

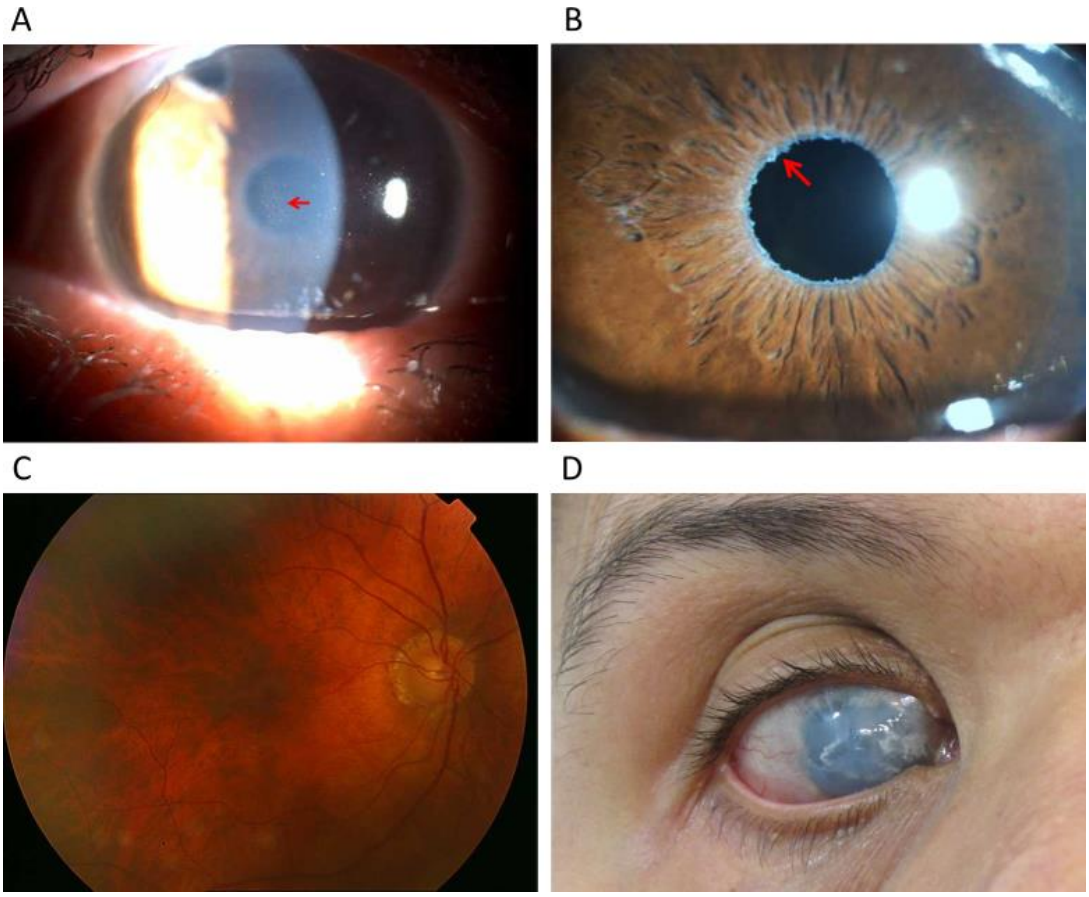
- The PXM deposition on trabecular meshwork increases the IOP, which is a greater risk factor for disease development. Hence, when the PXS is associated with increased and fluctuated IOP values, the PXFG is developed.[2,56]
- Whenever the increased IOP is sustained for a prolonged time, the optic nerve heads are damaged, characterized by loss of cells in retinal ganglions and causing related defects of visual fields. This condition is called glaucomatous optic neuropathy causing PXFG.[11]
- Other factors involved in PXS progression to glaucoma are the older age group population and the polymorphism of the LOXL1 gene. The association of PXS with systemic vascular diseases leads to disease progression. Environmental factors like geographic location and higher exposure to UV light can also progress PXS into PXFG.[3,11]

Pseudoexfoliative glaucoma (PXFG):

The PXFG is developed by the blockage of trabecular meshwork by the pseudoexfoliation materials, this promotes the deposition of cellular debris and pigment. The channel through which the aqueous humor outflows into Schlemm's canal can be blocked by these deposits. This may lead to IOP elevation and the development of PXFG.[1] The most common cause of secondary open-angle glaucoma is PXFG. It is associated with higher IOP, greater diurnal IOP fluctuations, and marked pressure spikes compared to primary open-angle glaucoma. The level of IOP and degree of pupil dilation play an important role in the formation of PXFG.[2] PXFG is more difficult to manage clinically and may require aggressive treatment to achieve target IOP levels. In PXFG, irreversible peripheral vision loss is caused by progressive damage and loss of retinal ganglion cells.[11] In comparison to POAG, the

PXFG has a worse prognosis because of its elevated IOP and poor response to medications. Hence the visual field and optic nerves were damaged rapidly corresponding to loss of vision. Therefore, this leads to surgical intervention. The major risk that causes PXFG is PXS.[57]

Figure 8: Eyes with pseudoexfoliation glaucoma: A) PXM deposition on the endothelial surface of the cornea, B) PXM deposition in the pupillary border of the iris, C) Glaucomatous optic neuropathy of fundus, D) Diffuse corneal opacity and calcified band keratopathy.[58]



Epidemiology:

About 50% of cases of pseudoexfoliation syndrome are attributed to pseudoexfoliation glaucoma.[29] PXFG accounts for about 25% of all open-angle glaucoma cases worldwide.[59] In South India, the PXFG prevalence is 1.6% to 4.7%.[21,60] Among the PXF patients reported in South India, the prevalence of glaucoma is 7.5% to 13%.[20,61] PXFG has a greater prevalence in Scandinavian countries and northern latitudes due to the high impact of UV exposure.[29,62] A study from Turkey reported that 26% of PXS patients are present with glaucoma.[63] The research from Croatia reported that 23.6% of PXS patients were affected by PXFG.[64] A study from the United States reported that 14.2% of PXS patients are diagnosed with glaucomatous damage. People above the age of 60 are highly affected by PXFG and those below 40 are uncommon. Female predominance is slightly higher.[29]

Etiopathogenesis:

The progressive accumulation of pseudoexfoliation material (PXM) in the trabecular meshwork and Schlemm's canal cells leads to increased outflow resistance. This, in turn, causes degenerative changes in Schlemm's canal and juxtacanalicular tissues, resulting in elevated intraocular pressure (IOP) and could cause PXFG.[2] The etiopathogenesis is associated with genetic factors, environmental and molecular factors.

- Genetic factors:

  The LOXL1 gene is the primary genetic factor in the development of PXFG. The variants of LOXL1 are strongly associated with PXFG. It is crucial in elastin metabolism, and the dysregulation causes alterations in ocular tissues, which leads to

disease development.[65] Dysregulation of LOXL1, TGF-β1 signalling, MMP/TIMP balance, and impaired autophagy all play critical roles in PXFG pathogenesis.[29] The contactin-associated protein-like 2 (CNTNAP2) gene is also associated.[38]

- Extracellular matrix (ECM) abnormalities:

  The PXM accumulation blocks the AH outflow, which leads to IOP elevation and glaucomatous damage. It is associated with higher diurnal variations, greater IOP, pressure spikes, rapid visual field loss, and severe optic neuropathy.[66] An increase in the level of oxidative markers and TGF-β1 in AH leads to the remodelling of ECM and IOP elevation.[29]

- Oxidative stress and Inflammation:

  The decrease in antioxidant levels and increase in markers of oxidative damage causes an increase in oxidative stress. This improves the PXM aggregation and causes damage to the ocular structure. Also, chronic inflammation is associated with PXFG development. In their tissues, proinflammatory cytokines are detected, which cause inflammatory components in disease formation.[65,66] The altered mitochondrial dysfunction is the important cause of PXFG formation.[67]

- Impaired cellular processes:

  The dysfunction of autophagic processes deposits the PXM and damages components of cells, leading to dysfunction of tissues and disease formation.[66]

- Vascular factors:

  Abnormality in vascular function develops the disease.[65]

Diagnosis:[29]

- Clinical examination:

- Slit lamp biomicroscopy visualizes the white flaky deposit (pseudoexfoliation material) in a bull's eye configuration of the lens capsule and iris transillumination defect due to stromal atrophy.
- The detection of heavily pigmented trabecular meshwork and the identification of the Sampaolesi's line can be done by gonioscopy.
- Measurement of IOP elevation and fluctuation.

❖ Imaging methods:

- Optic coherence tomography assesses the thinning of the nerve fiber layer and changes in the optic nerve head. Gives detailed information on the glaucomatous progression.
- The PXM deposit in the anterior chamber can be detected by ultrasound biomicroscopy or anterior segment OCT.

❖ Visual function test:

- Perimetry detects the defects of the glaucomatous visual field and monitors disease progression.

❖ Pachymetry assesses the central corneal thickness and thin corneas lead to underestimation of IOP in tonometry readings, thus it is helpful.

❖ Aqueous humor analysis.

❖ Differentiation of PXFG from other glaucomas.

Management:

Table 3: Management of Pseudoexfoliation glaucoma:[2,11,54,62]

Management Approach	Description	Key Considerations
Medical Management		
Prostaglandin Analogs	First-line therapy to lower IOP by increasing aqueous outflow.	Effective in reducing IOP spikes associated with PXG.
Beta-Blockers	Reduces aqueous humor production.	May have systemic side effects; contraindicated in asthma or cardiac conditions.
Carbonic Anhydrase Inhibitors	Decreases aqueous humor production.	Can be used as adjunctive therapy.
Alpha-Agonists	Reduces aqueous production and increases uveoscleral outflow.	Avoid in patients with cardiovascular concerns.
Combination Therapies	Utilized for better IOP control when monotherapy is insufficient.	E.g., beta-blocker + carbonic anhydrase inhibitor.
Laser Treatment		
Selective Laser Trabeculoplasty(SLT)	Non-invasive treatment to improve aqueous outflow through the trabecular meshwork.	Effective in PXFG due to increased trabecular pigmentation.
Argon Laser Trabeculoplasty	Similar to SLT but with a greater thermal effect.	May lead to scarring with repeated treatments.
Surgical Management		
Trabeculectomy	Creates an alternative drainage pathway for	High success rate, but increased risk of

	aqueous humor.	complications in PXFG due to inflammation and healing response.
Glaucoma Drainage Devices	Implantable devices which can divert aqueous humor to an external reservoir.	Preferred in patients with failed trabeculectomy or significant scarring.
Phacoemulsification with IOL	Cataract surgery combined with IOP-lowering procedures.	Addresses PXG-related lens changes and may improve IOP control.
Postoperative Management		
Anti-inflammatory Medications	Prolonged use of steroids to control postoperative inflammation.	Close monitoring to avoid steroid-induced IOP rise.

Complications of Pseudoexfoliative glaucoma:[29,68]

1. Progressive Optic Nerve Damage:

- When compared to primary open-angle glaucoma (POAG), PXFG can lead to rapid and aggressive optic nerve damage or cupping. If not managed properly or untreated it results in irreversible loss of vision.

2. Fluctuating and Elevated Intraocular Pressure (IOP):

- PXFG is characterized by highly variable and elevated IOP, which causes greater stress on the optic nerve. Difficulty in maintaining consistent IOP will raise the risk of glaucoma progression.

3. Corneal complications:[55]

- Decreased CCT and endothelial cell density predispose patients to corneal decompensation. The occurrence of oedema and damage in the cornea is higher, especially after surgical procedures.

4. Surgical challenges and risks:

- During surgeries like cataract extraction or trabeculectomy, PXFG patients have higher complications. Common issues include zonular instability leading to lens dislocation, capsular rupture during phacoemulsification, postoperative inflammation, and delayed recovery.

5. Angle-closure glaucoma:

- Narrowing or blockage of the anterior chamber angle can be caused by PXM and in severe cases may result in acute or chronic angle-closure glaucoma.

6. Postoperative complications:

- After surgeries like trabeculectomy or laser trabeculoplasty, there may be a risk of postoperative inflammation and IOP spikes. This likely results in scarring and failure of surgery due to the inflammatory response associated with PXFG.

7. Higher Risk of Vision Loss:

- As the disease progresses rapidly, PXFG patients are prone to an increased risk of severe visual loss or blindness. Delayed diagnosis from underestimated IOP readings in thinner corneas increases this risk.

AIMS & OBJECTIVES

AIMS & OBJECTIVES

AIM

To measure and correlate the diurnal variation in the central corneal thickness and intraocular pressure in Pseudoexfoliation eyes.

OBJECTIVES

- To assess central corneal thickness in Pseudoexfoliation eyes at 8 AM , 11AM , 2PM , 5 PM.
- To assess Intraocular Pressure in Pseudoexfoliation eyes at 8 AM , 11AM , 2PM , 5 PM.
- To compare and correlate between CCT and IOP in in Pseudoexfoliation eyes at 8 AM , 11AM , 2PM , 5 PM.

REVIEW OF

LITERATURE

REVIEW OF LITERATURE:

The prospective study of **Konstas A et al**.[69] (1995) assessed the diurnal (24-hours) IOP in PXFG patients. The study included 40 PXFG patients. The average age (in years) was 66. Males contribute 58%. The measurements were taken from 2 am to 10 pm. The average 2 am IOP (mmHg) was 27.6, which increased to 29.1 at 10 pm. The maximum IOP noted was 38.2 and the minimum was 24.7. The average range was 13.5.

The case-control study of **Ventura A et al.**[70] (1999) assessed the CCT in 13 PXFG patients and 21 healthy individuals. The average age was higher in PXFG patients than in healthy individuals (76 vs 58 years). The average CCT in PXFG (507) was decreased when compared to healthy individuals (524). The average IOP was higher in PXFG patients (21.6) when compared to healthy individuals (13.9).

Altintas et al.[71] (2001-2002) conducted a prospective study comparing the IOP variations for 24 hours in PXS patients (N= 19, 29 eyes) and healthy individuals (N= 25, 25 eyes). The average age (in years) was 67. The maximum average IOP (mmHg) in PXS patients was 19.47, and the minimum was 12.8. Whereas, the maximum average IOP (mmHg) in healthy individuals was 15.04, and the minimum was 11.6. The variations were significant ($p<0.05$). Among PXS patients, 55.6% resulted in a diurnal variation of > 5 mmHg. In 24 hours, higher IOP variations were seen in PXS patients than in healthy individuals.

Inoue K et al.[72] (2001) analysed the CCT changes in patients with pseudoexfoliation syndrome. This study included 21 PXS patients with 26 eyes and 30 healthy individuals with 30 eyes. Females were above 50%. The average age (in years) was

78. Among PXS patients, glaucoma was present in 33% (7/21). The CCT was significantly thinner in PXS patients (529 ± 31 μm) than in healthy people (547 ± 28 μm) (p= 0.03). When comparing PXS glaucoma patients (534 ± 37 μm), the CCT was lower in PXS non-glaucoma patients (528 ± 29 μm) and is insignificant (p >0.05).

Yagci R et al.[53] (2003) study was conducted on 25 PXFG patients and 50 healthy people. The average age was higher in PXFG patients than in healthy people (69 vs 47 years). Maximum females with 64% and 54% in PXFG and healthy people, respectively. In PXFG patients (17.5), the average IOP was higher than healthy people (15.6). The average CCT in PXFG patients and healthy individuals were 526.3 and 533.9 respectively but this was found to be insignificant (p=0.23). No significant correlation was found between IOP and CCT (p>0.05) in PXFG patients and healthy people.

The retrospective study of **Ozcura F et al**.[52] (2006-2009) examined 48 patients with 48 eyes. Among these, 40% (19/48) were present with glaucoma (PXFG), and 60% (29/48) were not present with glaucoma (PXF). Maximum females with 52%. The average age (in years) was 74. The average CCT in PXF patients (521) was significantly thinner than in PXFG patients (529.4) and healthy people (543.2) (p<0.05). The average IOP in PXF patients (13.8) was also lower than healthy people (14.9) and PXFG patients (19.7).

Kitsos G et al.[7] (2007-2008) in their cross-sectional study included 32 bilateral PXFG patients and 35 PXS patients. The average age (in years) was 71. Females contribute 53% and 51% of PXFG and PXS patient groups. The average IOP (mmHg) was higher in PXFG patients (15.7) than in PXS patients (13.9). In PXFG

patients (526), the average CCT (μm) was significantly thinner than in PXS patients (550.6) ($p<0.05$).

Tojo N et al.[73] (2012-2013) compared the IOP fluctuation between PXS patients and normal people using Triggerfish contact lens sensor (CLS). This cross-sectional study enrolled 11 PXS eyes and 11 healthy eyes. The male population is 64%. The average age (in years) was 72. The average CCT was thinner in PXS eyes (522 μm) than in healthy eyes (530 μm) and was not significant ($p=0.58$). The average IOP at baseline of PXS eyes (20.3 mmHg) was significantly higher than healthy eyes (13 mmHg) ($p<0.001$). The average IOP fluctuation seen during 24 hours was significantly higher in PXS eyes (502 mVeq) than in healthy eyes (294 mVeq) ($p=0.004$). The average IOP fluctuation of the diurnal period was significantly higher in PXS eyes (477 mVeq) than in healthy eyes (270 mVeq) ($p=0.006$). The average IOP fluctuation of the nocturnal period was also significantly higher in PXS eyes (272 mVeq) than in healthy eyes (179 mVeq) ($p=0.03$).

The prospective study of **Keel S et al**.[8] (2014) examined the diurnal variations of CCT and IOP in PXS patients. This study comprised 7 bilateral PXS patients with 14 eyes. Females contribute 71% (5/7). The average age (in years) was 70. They were measured from morning 8 am to evening 5 pm. In PXF patients, the average IOP (mmHg) in the right and left eyes at baseline were 17 and 15.7, which reduced to 12.9 and 11.9 in the evening, respectively. In PXF patients, the average CCT (μm) in the right and left eyes at baseline were 529.9 and 518.7, which reduced to 522.4 and 513.3 in the evening, respectively. The values were significant. A significant correlation was found between CCT and IOP. An average of 1 mmHg IOP increase

is associated with a 1.13 μm CCT increase. They noted that IOP decrease is correlated to CCT decrease.

Syed Z et al.[4] (2015-2017) evaluated patients with pseudoexfoliation syndrome (PXS) to analyze the central corneal thickness (CCT) and intraocular pressure (IOP) diurnal differences. This prospective observational study enrolled 85 patients with 141 eyes having PXS without glaucoma. Males contribute 73% (62/85). The average age (in years) was 63. The IOP and CCT were measured from morning, 8 am, to evening, 5 pm, in both eyes. The average IOP (mmHg) in the right and left eyes at baseline were 14.68 and 14.56, which significantly reduced to 13.26 and 13.18 in the evening, respectively ($p<0.001$). The average CCT (μm) in the right and left eyes at baseline were 514.95 and 513.47, which significantly reduced to 505.8 and 504.3 in the evening, respectively ($p<0.001$). During the daytime, the average IOP and CCT were significantly decreased by about 1.4 mmHg and 10 μm respectively. The variations in average IOP and CCT showed a positive correlation. As CCT decreased by 6.7 μm, there was an IOP reduction of 1mmHg on linear regression application.

The cross-sectional study of **Spoorthy et al.**[74] (2018) included 80 patients. Among these 50% (40/80) were healthy people and 50% (40/80) were PXF patients. Out of total PXF patients, 25% (10/40) had glaucoma. The average CCT was significantly higher in healthy people (549), compared to PXF patients (509) and PXF with glaucoma patients (498). Thus, patients with PXF show thinner CCT.

The prospective study of **Nanda P K et al**.[75] (2019) assessed 104 patients. The male population was 52%. Patients were between the ages of 50 and 70 years. Of total, 29% (30/104) had unilateral pseudoexfoliation (PXF), 3% (3/104) had bilateral PXF and 23% (24/104) had unilateral pseudoexfoliation glaucoma (PXFG). Healthy

individuals made up 45% (47/104) of the total. IOP and CCT were measured from 8 am to 5 pm. The average IOP in the morning (baseline) in healthy, PXF and PXFG patients was 15.17, 16.15, and 25.12, which significantly reduced to 13.55, 13.764, and 23.12 in the evening, respectively. Likewise, the average CCT in the morning (baseline) in healthy, PXF and PXFG patients were 530.8, 521.1, and 500.1 respectively and in the evening this was 525.45, 517.15, and 495.67 respectively, hence a significant reduction was noted ($p<0.05$). In PXFG patients, both IOP and CCT showed a significant decrease. Between IOP and CCT, a significant association was noted.

The cross-sectional study of **Sultana N et al.**[17] (2018-2019) enrolled 65 PXS and 65 PXFG patients. The average age (in years) was 68. Amongst a total of 130 patients, 68% of them were male. The IOP was between 10 to 21 mmHg in most of the patients with PXS, whereas the PXFG patients had an IOP of >21 mmHg. The average CCT PXS patients (511.5) was thinner when compared to PXFG patients (514.3) and healthy individuals (534.5). The CCT of PXS and PXFG patients showed no significance. But both were significant with healthy people.

Asritha et al.[76] (2018-2019) compared CCT between PXS and PXFG. This cross-sectional study comprised 210 subjects. Among these, 33% were PXS, 33% were PPXFG and 33% were healthy people. The average age was above 60 years in all the categories. Maximum males with 55%. The average CCT was significantly thinner in PXFG patients (515µm), compared to PXS patients (525µm) and healthy people (528µm) ($p=0.002$). The PXS patients (525µm) had thinner CCT than healthy people (528µm), which was not significant ($p=0.432$).

Ksheeraja Y et al.[6] (2021) compared CCT and IOP between PXF patients and non-PXF people (healthy). This prospective study enrolled 100 patients. Among these, 50% were PXF patients, and 50% were healthy people. The average age (in years) was 65. Maximum males with 61%. The average IOP in PXF patients (16.6) was significantly higher than healthy people (13.6) ($p<0.05$). The average CCT was significantly higher in healthy people (561) than PXF patients (536) ($p<0.05$). This study showed that there was a thinner cornea in PXF patients.

MATERIALS AND METHODS

MATERIALS AND METHODS

SOURCE OF DATA:

This Cross-sectional observational study included a total of 51 patients fulfilling the inclusion criteria in the Department of Ophthalmology, R.L.J. HOSPITAL AND RESEARCH CENTRE, attached to SRI DEVARAJ URS MEDICAL COLLEGE. Kolar

STUDY DESIGN: Cross-sectional Observational Study

PERIOD: May 2023 to October 2024

INCLUSION CRITERIA:

Patients above 40 years of equal gender with Pseudoexfoliation syndrome without glaucoma

EXCLUSION CRITERIA:

1. Diabetes mellitus
2. Corneal injuries
3. Corneal ectasia
4. Severe dry eye
5. Post keratorefractive surgeries
6. Uveitis
7. Glaucoma

ETHICAL CLEARANCE

Before the commencement, the study was approved by the Ethics and Research Committee, Sri Devraj Urs Medical College, Kolar.

INFORMED CONSENT

All the patients fulfilling selection criteria were explained about the nature of the study. A written informed consent was obtained from all the participants before enrolment (Annexure II)

METHOD OF COLLECTION OF DATA

A total of 51 eyes fulfilling the inclusion criteria were included in this prospective observational study. Each patient was assessed for demographic data, detailed history and clinical examination by the following methods:

1. Visual Acuity was done for both distant and near vision using Snellen's chart and Jaeger's chart respectively.

2. Slit lamp biomicroscopy to asses anterior chamber depth, any anterior segment abnormalities like corneal opacities, corneal oedema and keratoconus, presence of PEX material.

3. **Ultrasonic pachymetry:** The patient is made to sit comfortably on a chair, 0.5% procaine anaesthetic eyedrops are instilled into the eye and then the acquisition of corneal thickness is done. The probe of pachymetry is placed on the corneal surface centrally to obtain the CCT.

Fundus examination by direct and indirect ophthalmoscopy, including optic disc evaluation to see for any glaucomatous disc changes.

4. **Assessment of Intraocular Pressure using Goldmann Applanation Tonometer:** The patient is positioned at the slit lamp with their forehead against the headrest and instructed to look straight ahead. A topical anaesthetic and fluorescein are instilled into the conjunctival sac. With the cobalt blue filter in place and illumination at maximum intensity (angled 60°), the tonometer prism is centred on the corneal apex. The dial is preset at 10 mmHg, and the prism is advanced until it touches the cornea, creating two green semi-circular mires. The mire thickness should be about 10% of the arc's diameter. The dial is adjusted until the inner margins align, indicating a flattened area of 3.06 mm. The IOP is determined by multiplying the dial reading by 10.

5. Gonioscopy – Shaffer's grading system used

6. Humphery visual field analysis

TECHNIQUE

All subjects were assessed by four measurements of intraocular pressure and central corneal thickness during hospital hours on a single day at 4 sessions 8 AM, 11 AM, 2 PM and 5 PM by a single examiner to avoid any bias. Central corneal thickness was measured using ultrasound pachymetry and IOP was measured using a Goldmann applanation tonometer.

STATISTICAL METHODS USED FOR THIS STUDY

"Data was analysed using SPSS 22 version software after entering it into a Microsoft Excel datasheet. Representation of categorical data was done in the form of frequencies and proportions. As a test of significance for qualitative data, **the Chi-square test or Fischer's exact test** (for 2x2 tables only) was used. **Yates correction** was applied wherever chi-square rules were not fulfilled (for 2x2 tables only). Representation of continuous data was done using mean and standard deviation. **Independent t-tests or Mann Whitney U test** were used as tests of significance to identify the mean difference between two quantitative variables and qualitative variables respectively.

Graphical representation of data: MS Excel and MS Word were used to obtain various types of graphs such as bar and pie diagrams and scatter plots.

Pearson correlation or Spearman's correlation was done to find the correlation between two quantitative variables and qualitative variables respectively.

Correlation coefficient (r)	Interpretation
0 - 0.3	Positive Weak correlation
0.3-0.6	Positive Moderate correlation
0.6-1.0	Positive Strong correlation
0 to (-0.3)	Negative Weak correlation
(-0.3) to (-0.6)	Negative Moderate Correlation
(-0.6) to – (1)	Negative Strong Correlation

P-value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests"

Data Analysis

Data analysis was done in SPSS v27.0. Since the continuous variables were not normally distributed, the Spearman correlation was calculated. Friedman test was used to test the significance of the change of IOP and CCT over the time period. A p-value of less than 0.05 is taken as significant.

SAMPLE SIZE ESTIMATION

The sample size was estimated by using the correlation coefficient (r) of Mean IOP with Mean CCT as 0.53 (i.e. r = 0.53) from the study by Fogagnolo et al [12]. Using these values at a 99% confidence level and 90% power and substituting in the below formula, a sample size of 46 was obtained. Considering a 10% Non-response rate a sample size of 46 + 4.6 = 51 subjects will be included in the study.

Total sample size = N = $[(Z_\alpha+Z_\beta)/C]^2$ + 3

The standard normal deviate for $\alpha = Z_\alpha = 2.57$

The standard normal deviate for $\beta = Z_\beta = 1.28$

r = Correlation coefficient = 0.53

$C = 0.5 * \ln[(1+r)/(1-r)] = 0.5901$

RESULTS

RESULTS

The mean (SD) age of the patients in the study was 68.96 (9.08) years.

The median (IQR) age of the patients in the study was 69 (62,75) years

Most of the patients in the study were males (52.9%), while 47.1% were females.

Table 4: Statistical Analysis of the Subject Age

	Mean	Median	SD	IQR
AGE	68.96	69.00	9.08	62,75

Most of the patients in the study were males (52.9%), while 47.1% were females.

GENDER

Table 2:- Distribution of subjects according to gender

	Frequency	Per cent
Male	27	52.9
Female	24	47.1
Total	51	100.0

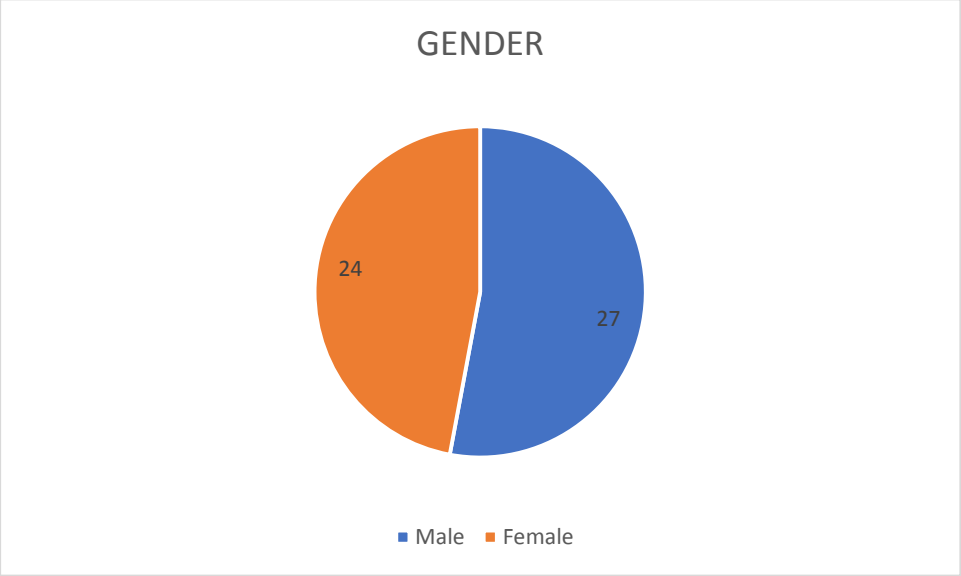


Figure 9: Sex distribution of the patients

The mean pre-op vision of the patients was 0.95 (log MAR)

The mean CCT at 8 AM, 11 AM, 2 PM and 5 PM were 524.22, 521.1, 520.37 and 515.51, respectively.

The mean IOP at 8 AM, 11 AM, 2 PM and 5 PM were 17.75, 17.55, 17.29 and 16.82, respectively.

Table 5 : Descriptive statistics of the vision, IOP and CCT of the patients

	Mean	Median	SD	IQR
PRE OP VISION	0.95	1.30	0.79	0.01,1.8
CCT 8AM	524.22	525.00	21.47	510,544
CORRECTED IOP 8 AM	17.75	18.00	3.76	14,21
CCT 11AM	521.10	530.00	20.73	503,538
CORRECTED IOP 11 AM	17.55	19.00	3.84	14,20
CCT 2 PM	520.37	527.00	20.74	506,536
CORRECTED IOP 2 PM	17.29	17.00	4.14	14,21
CCT 5 PM	515.51	520.00	17.51	510,526
CORRECTED IOP5 PMM	16.82	16.00	4.38	13,22

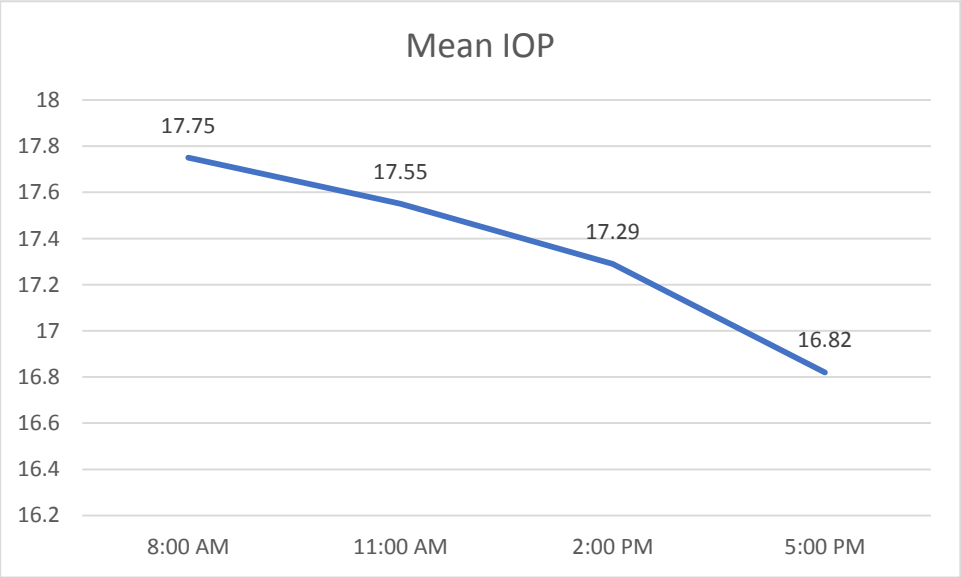


Figure 10 Mean IOP of patients at various time points

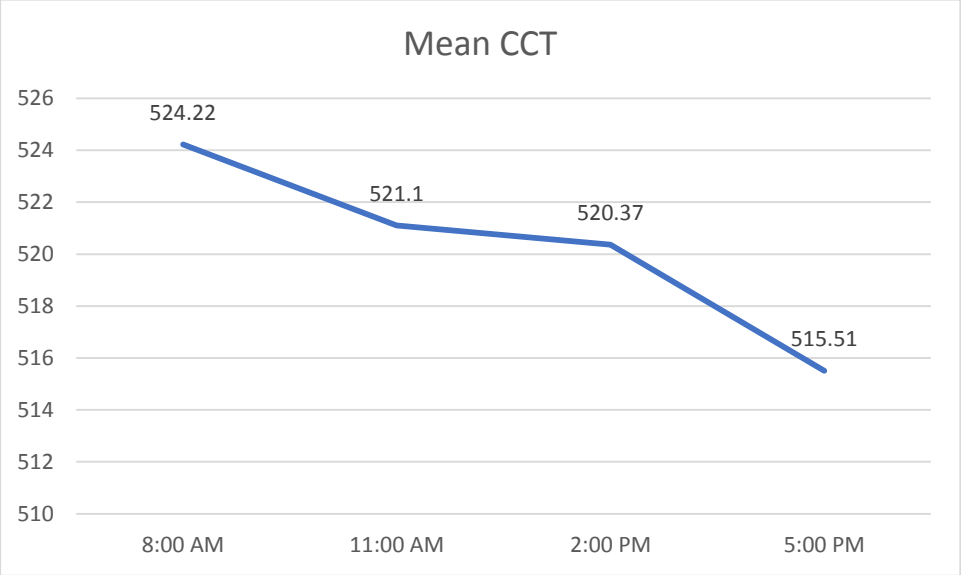


Figure 11:Mean CCT of patients at various time points

There was a significant negative correlation between CCT and IOP at all time points

Table 6: Correlation of CCT with IOP at various time points

Time	Rho (correlation co-efficient)	P value
8 AM	-0.598	<0.001
11 AM	-0.738	<0.001
2 PM	-0.562	<0.001
5 PM	-0.555	<0.001

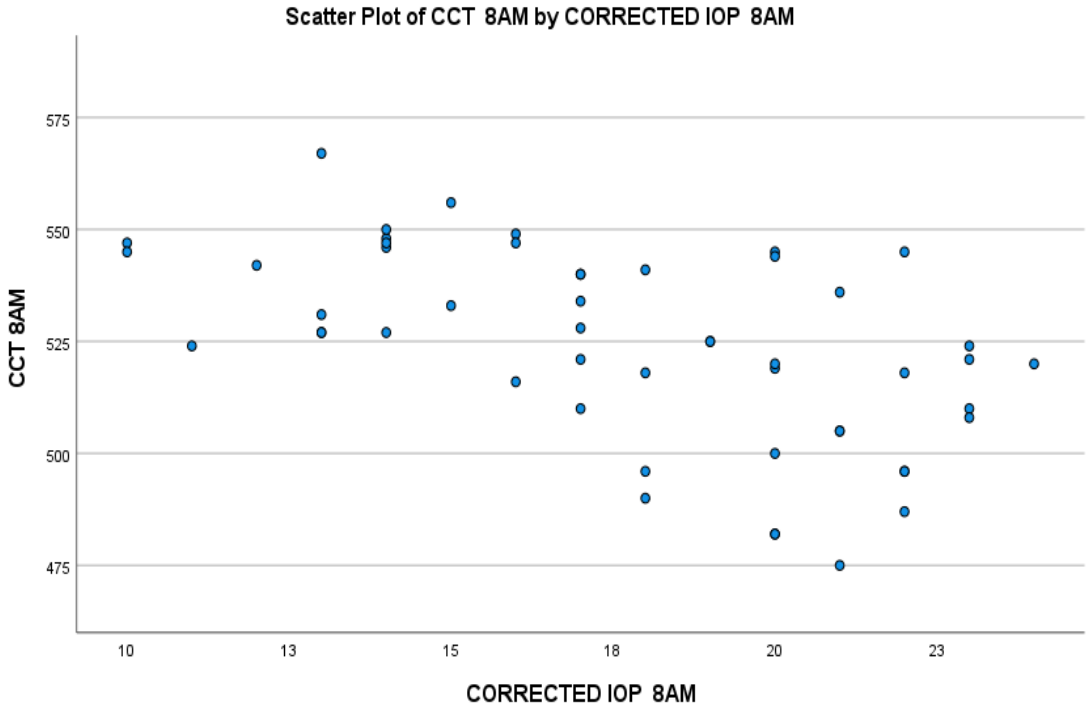


Figure 12: Scatter plot of CCT against corrected IOP at 8 AM

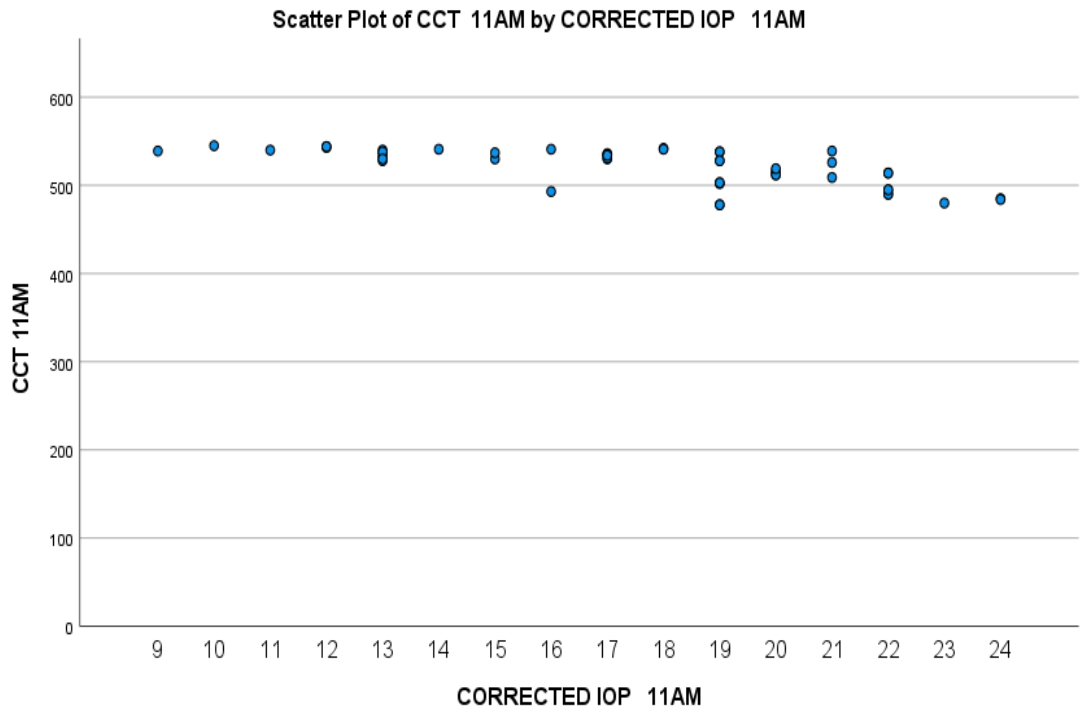


Figure 13: Scatter plot of CCT against corrected IOP at 11 AM

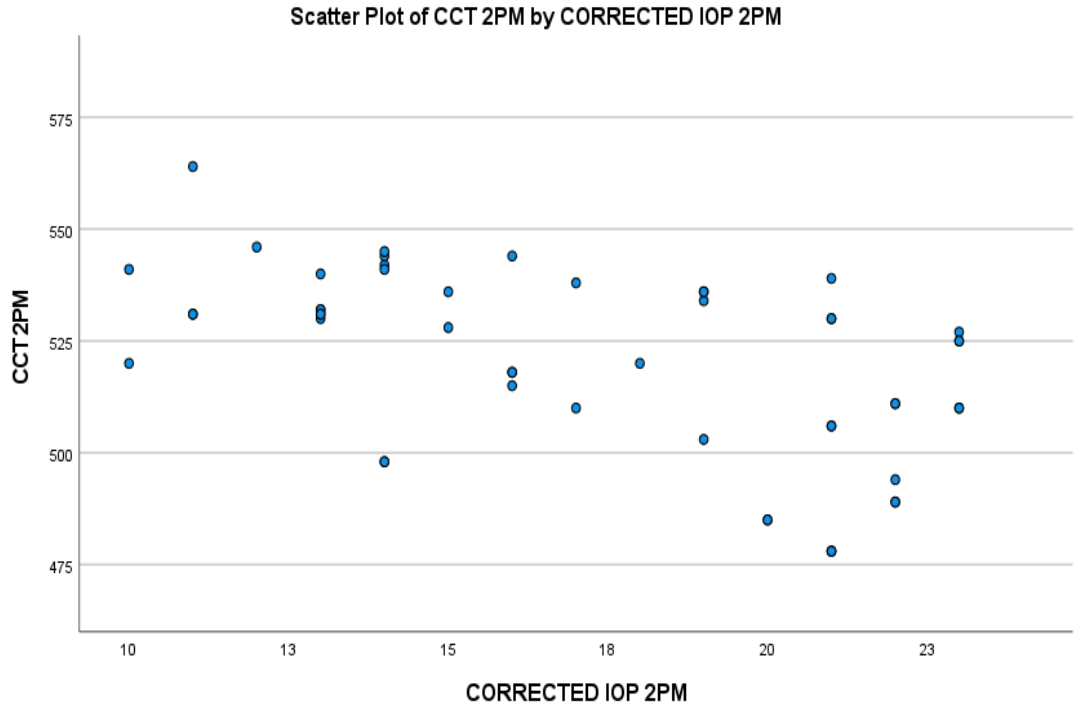


Figure 14: Scatter plot of CCT against corrected IOP at 2 PM

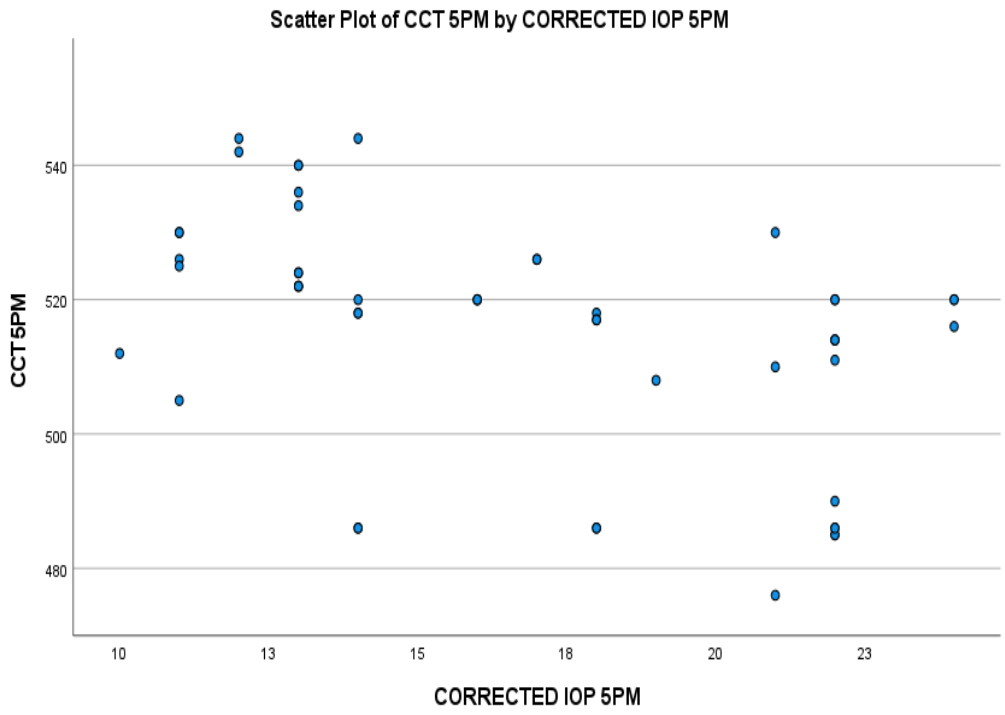


Figure 15: Scatter plot of CCT against corrected IOP at 5 PM

Table 7: Change in CCT over various time points of the day.

	Mean	Std. Deviation		
			Mean Rank	P value*
CCT 8 AM	524.22	21.470	3.10	<0.001
CCT 11AM	521.10	20.728	2.62	
CCT 2 PM	520.37	20.744	2.55	
CCT5 PMM	515.51	17.508	1.74	

*Friedman test

There was a significant decrease in CCT over the course of time in the day.

Table 8: Change in IOP over various time points of the day.

	Mean	Std. Deviation		
			Mean Rank	P value*
CORRECTED IOP 8 AM	17.75	3.762	2.83	0.110
CORRECTED IOP 11 AM	17.55	3.844	2.40	
CORRECTED IOP 2 PM	17.29	4.139	2.49	
CORRECTED IOP5 PMM	16.82	4.376	2.27	

*Friedman test

No significant variation in the IOP was observed in the patients over the period of time.

DISCUSSION

DISCUSSION

One of the leading preventable causes of blindness globally and in India is glaucoma. Pseudoexfoliation (PXF) is a generalized disorder and it is commonly age-related. It is often overlooked and may predispose to several ocular complications, especially glaucoma. In our study, we correlated the intraocular pressure and the diurnal variation in the central corneal thickness in Pseudoexfoliation eyes.

In our study, we included 51 Pseudoexfoliation eye conditions with an average age of 69 years with equal gender distribution. **Konstas A et al**.[69] included Pseudoexfoliation patients with 66 years, which is similar to our study. However, the average age (in years) was 74 in **Ozcura F et al**.[52] and 78 years in **Inoue K et al**.[72] which is higher than our study's average age of the study population.

Altintas et al.[71] estimated the IOP among PXF patients for diurnal variation including 67 years aged individuals. **Inoue K et al**.[72] (2001) analysed the CCT changes in patients with pseudoexfoliation and around 50% of the patients were females. **Ozcura F et al**.[52] similarly included 52% females. The gender distribution of the comparison studies was comparable to our study population inclusion.

To assess the diurnal variation, we assessed the CCT and IOP at 8 AM, 11 AM, 2 PM, and 5 PM. **Konstas A et al**.[69] estimated the variation at six time points in contrast to our study, i.e., at 2 AM, 6 AM, 10 AM, 2 PM, 6 PM, and 10 PM. This showed that the comparison study estimated the parameters more frequently and estimated change more frequently in comparison to our study. The IOP and CCT were measured from morning 8 am to evening 5 pm to estimate the diurnal variation

in the study of **Keel S et al**.[8] which is similar to the timing of the estimation of the parameters. The IOP and CCT were measured from morning, 8 am, to evening, 5 pm, in both eyes in the **Syed Z et al.**[4] study which has time points lesser than our study.

In our study, the mean CCT at 8 AM, 11 AM, 2 PM, and 5 PM were 524.22, 521.1, 520.37, and 515.51, respectively, i.e., gradually declined over the time period. On evaluation with statistical tests, the decline was significant across time points. **Inoue K et al**.[72] estimated the CCT as 529 ± 31 μm which is similar to our average estimates of CCT. The average CCT was thinner in PXF patients (526.3) in the study results of **Yagci R et al**.[53] which lies in the range of CCT of our study estimation of CCT.

The average CCT in PXF patients in **Ozcura F et al**.[52] was 521 which lies in the range of our study CCT results. **Kitsos G et al.**[7] documented an average CCT of 526 among the PXF with glaucoma eyes, which is similar to our study. The average CCT was thinner in PXS eyes (522 μm) than in healthy eyes (530 μm) in the study conducted by **Tojo N et al.**[73] The comparison study also estimated the change of CCT pre and post-surgery while we did not document the change in diurnal variation and its impact from the surgical procedure. **Keel S et al**.[8] documented a similar pattern of decline in CCT over the time points measured from 8 AM to 5 PM to estimate the diurnal variation i.e. the average CCT (μm) in the right and left eyes at baseline were 529.9 and 518.7, which reduced to 522.4 and 513.3 in evening.

Syed Z et al.[4] documented that the average CCT (μm) in the right and left eyes at baseline were 514.95 and 513.47, which significantly reduced to 505.8 and 504.3 in the evening, respectively, which is similar to the declining pattern of CCT in our

study. The similarity in pattern might be due to the estimation of the CCT values at the same time points, i.e., 8 AM and 5 PM, in both studies. This pattern may be explained by corneal hydration dynamics, where overnight corneal swelling due to closed-eye conditions is followed by gradual thinning throughout the day as the eye is exposed to ambient conditions and blinking, which helps in fluid redistribution and evaporation.

Spoorthy et al.[74] in their study noted the CCT of PXF patients (509) and PXF with glaucoma patients (498) without estimating the change in the diurnal variation. Thinning of the CCT was pronounced in the comparison study with 25% of PXF patients having glaucoma. However, we did not stratify the PXF with glaucoma to compare the change in the CCT values. The average CCT in the baseline among the PXF and PXFG patients was 521.1, and 500.1, which significantly reduced to 517.1, and 495.6 in the evening in the study results of **Nanda P K et al**.[75] The parameters were similar and comparable to the reduction pattern our study. **Sultana N et al.**[17] estimated the average CCT was thinner in PXS patients (511.5), compared to PXFG patients (514.3) in which the CCT parameters were comparable to our study results. A similar observation was documented in the study conducted by **Asritha et al.**[76] where the PXS patients (525µm) had thinner CCT comparable to our study results.

In our study, the mean IOP at 8 AM, 11 AM, 2 PM, and 5 PM were 17.75, 17.55, 17.29, and 16.82, respectively, with a decline over time points, but the difference was not significant. This pattern aligns with the known physiological rhythm of IOP, which typically peaks in the early morning and gradually decreases as the day progresses due to factors such as changes in aqueous humor dynamics, body posture, and hormonal influences. However, the lack of statistical significance in our findings

may be attributed to factors such as sample size, individual variability, or the relatively small magnitude of IOP change over the day. The average IOP (mmHg) at 2 am was 27.6, which increased to 34.8 at 10 AM and thereafter declined to 29.1 at 10 PM in **Konstas A et al**.[69] study. The IOP values were higher than those in our study, and the difference might be due to variations in the study population (Greek professional population). The average IOP was higher in PXF patients was 21.6 in the study results of **Ventura A et al.**[70] probable because of the single time estimate of the IOP in comparison to the diurnal variation estimation. The study by **Altintas et al**.[71] documented that the diurnal variation of IOP ranged from 23.8 to 19.4 and this was wider in interval than our findings of mean IOP. **Yagci R et al**.[53] estimated an average IOP of 17.5, which is in the range of the estimates of diurnal variation in our study findings.

The average IOP in PXF patients in **Ozcura F et al**.[52] was 13.8, which is lower than our study population. However, it was higher for those with PXF with glaucoma(19.7). This states that the PXF with glaucoma had a higher chance of having higher IOP in comparison to the healthy and PXF eyes. Similar documentation was done in the study conducted by **Kitsos G et al.**[7] who observed that the average IOP (mmHg) was higher in PXFG patients (15.7) than in PXS patients (13.9). In PXF patients, the average IOP (mmHg) in both eyes at baseline was 15.7-17, which was reduced to 11.9-12.9 in the evening, respectively in the study results of **Keel S et al**.[8] Though the decline in the IOP pattern was similar to our study, the estimate of average IOP at all time points was lower than our study which indicates that the severity of intraocular pressure was higher in our study. The average IOP (mmHg) in the right and left eyes at baseline were 14.68 and 14.56, which significantly reduced to 13.26 and 13.18 in the evening in the **Syed Z et al.**[4]

study. However, the IOP values were higher in our study in comparison, meanwhile, the declining pattern of IOP was similar in both studies.

The average IOP in the baseline among the PXF and PXFG patients was 16.15 and 25.12, which significantly reduced to 13.7, and 23.1 in the evening in the study results of **Nanda P K et al**.[75] The parameters were similar and comparable to the reduction pattern our study.

A significant negative correlation was noted between CCT and IOP at all time points. However, **Yagci R et al**.[53] did not observe any significant correlation, probably because of the lower sample size in the comparison study 25 eyes which is half that of the study population of our study. In contrast to our study, **Keel S et al**.[8] documented a positive correlation between the CCT and IOP i.e. 1 mmHg increase in IOP was observed if the CCT increased by 1.13 units, while we documented a negative correlation between CCT and IOP. The difference might be due to reasons such as variation in sample size (14 eyes in the comparison study). The negative correlation in our study might be due to biomechanical properties of the cornea influencing the accuracy of IOP measurements such as Measurement artifacts, physiological differences, Corneal biomechanics and ocular rigidity and population-specific factors.

Most tonometers, particularly Goldmann Applanation Tonometers, are calibrated based on a standard corneal thickness of approximately 520 μm. Greater force is required to flatten the cornea in cases where it is thicker and this can lead to overestimation of IOP. Conversely, the IOP values may be underestimated in thinner corneas since they require less force. However, in our study, the negative correlation suggests that with increasing CCT, IOP readings decreased, which is contrary to

expected measurement artifacts. This indicates that additional factors beyond tonometric assumptions may be influencing the results. It is possible that eyes with thinner corneas inherently have higher true IOP values or possess different biomechanical properties. For instance, thinner corneas may exhibit reduced corneal hysteresis or structural rigidity, which could alter the cornea's response to intraocular pressure and influence both actual pressure and how measurement tools detect it.

The corneal thickness is closely related to its biomechanical behaviour. Thinner corneas may represent eyes with lower structural integrity or elasticity, which can influence how pressure is transmitted and measured. On the other hand, thicker or more rigid corneas might absorb more of the pressure exerted by the tonometer, resulting in lower measured IOP despite higher actual pressure. These biomechanical variations could contribute to the inverse relationship found in our data.

LIMITATIONS:

- Our study was conducted as an observational pattern without estimating the effect of any intervention
- The follow-up of patients with a change in diurnal variation based on the management was not assessed
- The external validity of other settings is limited for the study population younger than the study population of our study.
- The study was cross-sectional and did not assess long-term changes or progression of IOP and CCT over days, weeks, or months.
- Absence of a Control Group - No comparison was made with a healthy population or other types of glaucoma, limiting the ability to contextualize the findings specifically to PXS.
- The study included PXS patients but did not differentiate between those with and without pseudoexfoliation glaucoma (PXFG), which may have different IOP and CCT profiles.
- Measurements were only taken four times during the day (8 AM, 11 AM, 2 PM, and 5 PM), potentially missing early morning or late-night peaks in IOP that are common in glaucoma.

STRENGTHS OF THE STUDY :

- The study addresses diurnal variations in IOP and CCT in pseudoexfoliation syndrome (PXS) — a topic with significant implications for glaucoma diagnosis and management.
- By measuring IOP and CCT at four time points during the day, the study provides a dynamic profile of these parameters rather than relying on a single snapshot.
- The study evaluates both IOP and CCT in tandem, allowing for analysis of their correlation, which is important for accurate glaucoma risk assessment.
- Since the study was conducted in a routine ophthalmic care centre, it reflects a practical and applicable setting, making findings more relatable to day-to-day clinical care.

CONCLUSION

CONCLUSION

Accurate measurement of intraocular pressure and central corneal thickness (CCT) is essential for timely diagnosis and effective management, especially considering their diurnal variability. In our study, we observed a significant decline in central corneal thickness in the diurnal variation assessment among patients with pseudoexfoliation eyes. Similarly, there was a decline in the intraocular pressure however the decline was insignificant. We concluded that there was a negative correlation between the CCT and IOP at individual time point assessments. These findings underscore the importance of considering time of day and corneal characteristics when evaluating IOP in PXF patients. Further studies with longitudinal follow-up need to be conducted to estimate the change in diurnal variation compared with the various management procedures.

The results of this study show that single-time-point assessments of IOP and CCT may be insufficient in patients with PXS and that the possibility of diurnal variation should be considered when making diagnosis and management decisions. Moreover, the findings emphasize the necessity of regular and comprehensive monitoring, particularly in patients with known or suspected glaucoma risk, to better understand the physiological fluctuations and their implications.

In conclusion, this study contributes valuable insights into the ocular behaviour of pseudoexfoliation syndrome, particularly in terms of IOP and CCT fluctuations. The evidence supports the integration of time-of-day considerations into routine clinical practice and encourages further research into how these variations can be incorporated into individualized patient management plans. Future longitudinal studies and investigations into the biomechanical properties of the PXS cornea may

help to refine diagnostic accuracy and therapeutic approaches, ultimately improving outcomes for patients affected by this complex disorder.

SUMMARY

SUMMARY

- The research aims to evaluate diurnal variations in intraocular pressure (IOP) and central corneal thickness (CCT) in eyes with pseudoexfoliation syndrome (PXS), which can contribute to glaucoma progression.
- IOP and CCT both fluctuate throughout the day, and these fluctuations are often exaggerated in PXS, impacting diagnosis and management.
- 51 patients with PXS were involved in the observational study. Measurements for IOP and CCT were taken at 8 AM, 11 AM, 2 PM, and 5 PM.
- It was conducted among the patients visiting the outpatient Ophthalmology department at R.L.J. Hospital And Research Centre, Sri Devaraj Urs Medical College between May 2023 to October 2024.
- The mean age was approximately 69 years, with a slightly higher number of male patients (52.9%).
- Mean CCT declined significantly throughout the day: from 524.22 µm at 8 AM to 515.51 µm at 5 PM, indicating a significant diurnal thinning.
- Mean IOP also declined slightly, from 17.75 mmHg at 8 AM to 16.82 mmHg at 5 PM, but this decline was not statistically significant.
- A significant negative correlation was found between CCT and IOP at all time points ($p < 0.001$), suggesting that as the cornea thins, IOP tends to decrease.
- The findings were consistent with several past studies that reported thinner CCT and higher IOP in PXS and PXFG patients compared to healthy individuals.
- Thinner CCT can lead to underestimation of IOP, possibly delaying glaucoma diagnosis or leading to inadequate treatment.

- Since CCT influences IOP readings, routine monitoring of both is essential for accurate glaucoma risk assessment in PXS.
- The mild decline in IOP is aligned with a known circadian rhythm, typically peaking in the morning and decreasing through the day.
- In conclusion, the study emphasizes the importance of time-of-day considerations and individual corneal characteristics in assessing IOP and managing PXS to make an early diagnosis of glaucoma and prevent its progression.

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ANNEXURE

ANNEXURE-1

CASE PROFORMA

Name:	Case No:
Age:	Date:
Sex:	1P No:
Occupation:	DOE:
Address:	

Chief complaints:

Past history:

DM / HTN / BA / Epilepsy

Family history:

Personal history:

Appetite – Sleep – Bowel –

Diet – Habits – Bladder –

GPE:

Pallor / Edema /Icterus / Cyanosis / Clubbing / Lymphadenopathy

Vital signs:

Pulse – c) RR –

BP – d) Temp –

Systemic examination:

CVS – c. RS –

PA – d. CNS –

OCULAR EXAMINATION		
	OD	**OS**
Head posture **Ocular posture** **Facial symmetry**		
Ocular movements		
Visual acuity: Distant Near		
ANTERIOR SEGMENT		
FUNDUS (IDO & Slit Lamp +90D)		
INTRAOCULAR PRESSURE (mmHg)		
AXIAL LENGTH (mm)		
. IOL Power		
. GONISCOPY		
. CCT		

ANNEXURE-II

INFORMED CONSENT FORM

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.

Case no:

IP no:

TITLE: EVALUATION OF DIURNAL VARIATION OF INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS IN PSEUDOEXFOLIATION EYES

I, the undersigned, agree to participate in this study and authorize the collection and disclosure of personal information as outlined in this consent form.

I understand the purpose of this study, the risks and benefits of the technique and the confidential nature of the information that will be collected and disclosed during the study. The information collected will be used only for research.

I have had the opportunity to ask questions regarding the various aspects of this study and my questions have been answered to my satisfaction.

I understand that I remain free to withdraw my participation from this study at any time and this will not change my future care.

Participation in this study does not involve any extra cost to me.

Name	Signature	Date	Time
Patient:			
Witness:			
Primary Investigator/ Doctor:			

ಶ್ರೀದೇವರಾಜ್ಅರಸ್ಉನ್ನತಶಿಕ್ಷಣಮತ್ತುಸಂಶೋಧನಾಸಂಸ್ಥೆ, ಟಮಕ, ಕೋಲಾರ - 563101.

ತಿಳಿವಳಿಕೆಸಮ್ಮತಿನಮೂನೆ

ಶೀರ್ಷಿಕೆ: "ಇಂಟ್ರಾಕ್ಯುಲರ್ ಒತ್ತಡದ ದೈನಂದಿನ ಬದಲಾವಣೆಯ ಮೌಲ್ಯಮಾಪನ ಮತ್ತು ಹುಸಿ ಎಕ್ಸ್ಫೋಲಿಯೇಶನ್ ಕಣ್ಣುಗಳಲ್ಲಿ ಕೇಂದ್ರ ಕಾರ್ನಿಯಲ್ ದಪ್ಪ"

ಐಪಿ ಸಂಖ್ಯೆ:

ಅಂಗೀಕರಿಸಿದ ನಾನು, ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ಒಪ್ಪುತ್ತೇನೆ ಮತ್ತು ಈ ಸಮ್ಮತಿಯ ರೂಪದಲ್ಲಿ ವಿವರಿಸಿರುವಂತೆ ನನ್ನ ವೈಯಕ್ತಿಕ ಮಾಹಿತಿಯ ಸಂಗ್ರಹಣೆ ಮತ್ತು ಬಹಿರಂಗಪಡಿಸುವಿಕೆಯನ್ನು ದೃಢೀಕರಿಸುತ್ತೇನೆ.

ನಾನು ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶ, ತಂತ್ರಗಳ ಅಪಾಯಗಳು ಮತ್ತು ಪ್ರಯೋಜನಗಳನ್ನು ಮತ್ತು ಅಧ್ಯಯನದಲ್ಲಿಸಂಗ್ರಹಿಸಿದ ಮತ್ತು ಬಹಿರಂಗಪಡಿಸುವ ಮಾಹಿತಿಯ ಗೌಪ್ಯತೆಗೆ ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಸಂಗ್ರಹಿಸಿದ ಮಾಹಿತಿಯನ್ನು ಸಂಶೋಧನೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.

ಈ ಅಧ್ಯಯನದ ವಿವಿಧ ಅಂಶಗಳನ್ನು ಕುರಿತು ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶವಿದೆ ಮತ್ತು ನನ್ನ ತೃಪ್ತಿಗೆ ನನ್ನ ಪ್ರಶ್ನೆಗಳಿಗೆ ಉತ್ತರ ನೀಡಲಾಗಿದೆ.

ಈ ಸಂಶೋಧನೆಯಿಂದ ಹೊರಬರುವ ಮಾಹಿತಿಯನ್ನು ವೈದ್ಯರು ಯಾವುದೇ ಜರ್ನಲ್ನಲ್ಲಿ ಅಥವಾ ಕಾನ್ಫೆರೆನ್ಸ್ನಲ್ಲಿ ಪ್ರಕಟಿಸಲು ಅನುಮತಿ ಸೂಚಿಸಿರುತ್ತೇನೆ

ನಾನು ಈ ಅಧ್ಯಯನದಿಂದ ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಹಿಂತೆಗೆದುಕೊಳ್ಳಲು ಮುಕ್ತವಾಗಿರುತ್ತೇನೆ ಮತ್ತು ಇದು ನನ್ನ ಮುಂದಿನ ಕಾಳಜಿಯನ್ನು ಬದಲಿಸುವುದಿಲ್ಲ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಈ ಸಂಶೋಧನಾ ಯೋಜನೆಯ ಭಾಗವಹಿಸುವಿಕೆ ನನಗೆ ಯಾವುದೇ ಹಣಕಾಸಿನ ಹೊರೆ ಒಳಗೊಂಡಿರುವುದಿಲ್ಲ.

ಹೆಸರು	ಸಹಿ	ದಿನಾಂಕ	ಸಮಯ
ರೋಗಿಯ:			
ಸಾಕ್ಷಿ 1:			
ಸಾಕ್ಷಿ 2:			
ಪ್ರಾಥಮಿಕ ತನಿಖೆದಾರ / ಡಾಕ್ಟರ್:			

ANNEXURE-III

PATIENT INFORMATION SHEET

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.

TITLE:" EVALUATION OF DIURNAL VARIATION OF INTRAOCULAR PRESSURE AND CENTRAL CORNEAL THICKNESS IN PSEUDOEXFOLIATION EYES"

This information is to help you understand the purpose of the study "**Evaluation Of Diurnal Variation Of Intraocular Pressure And Central Corneal Thickness In Pseudoexfoliation Eyes** "

You are invited to take part voluntarily in this research study, it is important that you read and understand the purpose, procedure, benefits and discomforts of the study.

This study is done to measure the Intraocucplar Pressure And Central Corneal Thickness at different time intervals during the day (8 am, 11 am, 2 pm, 5 pm). This data can be used to predict if you are prone to glaucoma in the future and can plan appropriate treatment courses.

To measure the Central Corneal Thickness & Intra Ocular Pressure, the patient is made to sit in front of the ultrasound pachymeter & Goldmann Applanation Tonometer after applying topical anaesthetic drops and the value is measured. There are no risks associated with the various investigations to be done which include routine ophthalmic examination procedures.

Participation in this research study may not change the outcome of your eye condition. However, patients in the future may benefit as a result of knowledge

gained from this study. You will not be charged extra for any of the procedures performed during the research study. Your taking part in this study is entirely voluntary.

You may refuse to take part in the study or you may stop your participation in the study at any time, without any penalty or loss of any benefits to which you were otherwise entitled before taking part in this study.

CONFIDENTIALITY

Your medical information will be kept confidential by the study doctor and staff and will not be made publicly available. Your original records may be reviewed by your doctor or ethics review board.

For further information,/clarification please contact Dr. Alisha Elizabeth Alex , SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR – 563101.Contact no: 9094219684

ಶೀರ್ಷಿಕೆ: " ಶೀರ್ಷಿಕೆ:'' ಇಂಟ್ರಾಕ್ಯುಲರ್ ಒತ್ತಡದ ದೈನಂದಿನ ಬದಲಾವಣೆಯ ಮೌಲ್ಯಮಾಪನ ಮತ್ತು ಹುಸಿ ಎಕ್ಸ್ಫೋಲಿಯೇಶನ್ ಕಣ್ಣುಗಳಲ್ಲಿ ಕೇಂದ್ರ ಕಾರ್ನಿಯಲ್ ದಪ್ಪ''

ಈ ಮಾಹಿತಿಯು ನಿಮಗೆ ಅಧ್ಯಯನದ ಉದ್ದೇಶವನ್ನು ಅರ್ಥಮಾಡಿಕೊಳ್ಳಲು ಸಹಾಯ ಮಾಡುತ್ತದೆ " ಇಂಟ್ರಾಕ್ಯುಲರ್ ಒತ್ತಡದ ದೈನಂದಿನ ಬದಲಾವಣೆಯ ಮೌಲ್ಯಮಾಪನ ಮತ್ತು ಹುಸಿ ಎಕ್ಸ್ಫೋಲಿಯೇಶನ್ ಕಣ್ಣುಗಳಲ್ಲಿ ಕೇಂದ್ರ ಕಾರ್ನಿಯಲ್ ದಪ್ಪ''

ಈ ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಪಾಲ್ಗೊಳ್ಳಲು ನಿಮ್ಮನ್ನು ಆಹ್ವಾನಿಸಲಾಗಿದೆ, ನೀವು ಅಧ್ಯಯನದ ಉದ್ದೇಶ, ಕಾರ್ಯವಿಧಾನ, ಪ್ರಯೋಜನಗಳು ಮತ್ತು ಅನಾನುಕೂಲಗಳನ್ನು ಓದುವುದು ಮತ್ತು ಅರ್ಥಮಾಡಿಕೊಳ್ಳುವುದು ಮುಖ್ಯವಾಗಿದೆ.

ಇಂಟ್ರಾಕ್ಯುಲರ್ ಪ್ರೆಶರ್ ಮತ್ತು ಸೆಂಟ್ರಲ್ ಕಾರ್ನಿಯಲ್ ದಪ್ಪವನ್ನು ದಿನದ ವಿವಿಧ ಸಮಯಗಳಲ್ಲಿ (8am,11am,2pm , 5pm) ಅಳೆಯಲು ಈ ಅಧ್ಯಯನವನ್ನು ಮಾಡಲಾಗುತ್ತದೆ .ಈ ಡೇಟಾವನ್ನು ನೀವು ಭವಿಷ್ಯದಲ್ಲಿ ಗ್ಲುಕೋಮಾಗೆ ಗುರಿಯಾಗುತ್ತೀರಾ ಎಂದು ಊಹಿಸಲು ಬಳಸಬಹುದು ಮತ್ತು ಸೂಕ್ತವಾದ ಯೋಜನೆ ಮಾಡಬಹುದು ಚಿಕಿತ್ಸೆಯ ಕೋರ್ಸ್.ಕೇಂದ್ರ ಕಾರ್ನಿಯಲ್ ದಪ್ಪ ಮತ್ತು ಇಂಟ್ರಾ ಆಕ್ಯುಲರ್ ಪ್ರೆಶರ್ ಅನ್ನು ಅಳೆಯಲು, ರೋಗಿಯನ್ನು ಅಲ್ಟ್ರಾಸೌಂಡ್ ಪ್ಯಾಚಿಮೀಟರ್ ಮತ್ತು ಗೋಲ್ಡ್ಮನ್ ಅಪ್ಲನೇಷನ್ ಟೋನೋಮೀಟರ್‌ನ ಮುಂದೆ ಕುಳಿತುಕೊಳ್ಳುವಂತೆ ಮಾಡಲಾಗುತ್ತದೆ ಮತ್ತು ಸಾಮಯಿಕ ಅರಿವಳಿಕೆ ಹನಿಗಳನ್ನು ಅನ್ವಯಿಸಿದ ನಂತರ ಮೌಲ್ಯವನ್ನು ಅಳೆಯಲಾಗುತ್ತದೆ.

ನಾವು ಸ್ಕಿರ್ಮರ್ಸ್ ಪರೀಕ್ಷೆ, ಕಣ್ಣೀರಿನ ಚಲನಚಿತ್ರವು ಸಮಯವನ್ನು ಮುರಿಯುತ್ತದೆ. ವಾಡಿಕೆಯ ನೇತ್ರ ಪರೀಕ್ಷೆಯ ಕಾರ್ಯವಿಧಾನಗಳನ್ನು ಒಳಗೊಂಡಿರುವ ವಿವಿಧ ತನಿಖೆಗಳಿಗೆ ಸಂಬಂಧಿಸಿದ ಯಾವುದೇ ಅಪಾಯಗಳಿಲ್ಲ.

ಅಂತಹ ತೊಡಕುಗಳನ್ನು ಅವನು ಗುರುತಿಸುವುದು ಅಥವಾ ಅಭಿವೃದ್ಧಿ ಹೊಂದುವ ಅಪಾಯವು ಅದರ ಸಂಭವವನ್ನು ಕಡಿಮೆ ಮಾಡಲು ಬೇಕಾದ ಬದಲಾವಣೆಗಳ ನಿರ್ಣಯದಲ್ಲಿ ಮಹತ್ವದ್ದಾಗಿರುತ್ತದೆ, ಹೀಗಾಗಿ ತೀವ್ರವಾದ ಆಕ್ಯುಲರ್ ಆವಿಷ್ಕಾರದ ಹೊರೆಯನ್ನು ಕಡಿಮೆ ಮಾಡುತ್ತದೆ ನಮ್ಮ ವೀಕ್ಷಣೆ ಸಹ ಪ್ರಾಮುಖ್ಯತೆಯನ್ನು ಹೊಂದಿರಬಹುದು.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಪಾಲ್ಗೊಳ್ಳುವಿಕೆಯು ಸಂಪೂರ್ಣವಾಗಿ ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ. ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನೀವುನಿರಾಕರಿಸಬಹುದು ಅಥವಾ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವುದಕ್ಕಿಂತ ಮೊದಲು

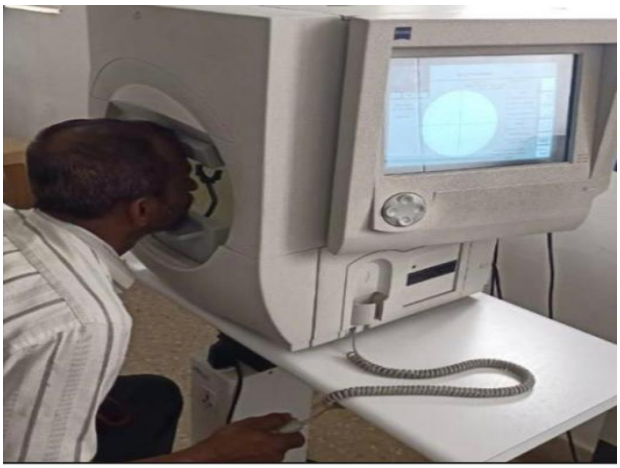
ನೀವುಯಾವುದೇ ಅರ್ಹತೆಗೆ ಯಾವುದೇ ದಂಡವಿಲ್ಲದೆ ಅಥವಾ ನಷ್ಟವಿಲ್ಲದೆಯೇ ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಭಾಗವಹಿಸುವಿಕೆಯನ್ನುನಿಲ್ಲಿಸಬಹುದು. ಈ ಸಂಶೋಧನೆಯಿಂದ ಹೊರಬರುವ ಮಾಹಿತಿಯನ್ನು ವೈದ್ಯರು ಯಾವುದೇ ಕಾನ್ಫೆರೆನ್ಸ್ನಲ್ಲಿ ಪ್ರಕಟಿಸಲು ಅನುಮತಿ ಸೂಚಿಸಿರುತ್ತೇನೆ

ಗೌಪ್ಯತೆ

ನಿಮ್ಮ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿಯನ್ನು ಅಧ್ಯಯನದ ವೈದ್ಯರು ಮತ್ತು ಸಿಬ್ಬಂದಿ ಗೌಪ್ಯವಾಗಿಡಲಾಗುವುದು ಮತ್ತು ಸಾರ್ವಜನಿಕವಾಗಿ ಲಭ್ಯವಿರುವುದಿಲ್ಲ. ನಿಮ್ಮ ಮೂಲದಾಖಲೆಗಳನ್ನು ನಿಮ್ಮ ವೈದ್ಯರು ಅಥವಾ ನೈತಿಕ ವಿಮರ್ಶೆ ಮಂಡಳಿ ಪರಿಶೀಲಿಸಬಹುದು.

ಹೆಚ್ಚಿನ ಮಾಹಿತಿಗಾಗಿ,/ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ದಯವಿಟ್ಟು ಡಾ. ಅಲಿಶಾ ಎಲಿಜಬೆತ್ ಅಲೆಕ್ಸ್, ಶ್ರೀ ದೇವರಾಜ್ ಯುಆರ್ಎಸ್ ಉನ್ನತ ಶಿಕ್ಷಣ ಮತ್ತು ಸಂಶೋಧನೆ ಅಕಾಡೆಮಿ, ತಮಕ, ಕೋಲಾರ – 563101.ಸಂಪರ್ಕ ಸಂಖ್ಯೆ: 9094219684

ANNEXURE-IV



PHOTOGRAPH 1 : HUMPHREYS VISUAL FIELD ANALYSER

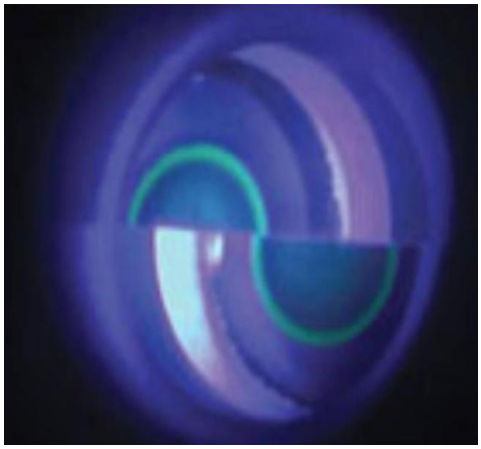
PHOTOGRAPH 2:

GONIOSCOPY

PHOTOGRAPH 3:

GOLDMANN APPLANATION TONOMETRY

PHOTOGRAPH 4: RE- CCT MEASUREMENT BY ULTRASONIC PACHYMETRY



PHOTOGRAPH 5: SLIT LAMP OCULAR VIEW OF FLUORESCEIN SEMICIRCLES INDICATING IOP DURINGAPPLANATION TONOMETRY.

MASTER CHART

UHID	AGE	GENDER	PRE OP VISION		CATARACT GRADING	PEX	8AM			11AM			2PM			5PM		
							IOP	CCT	CORRECTED IOP	IOP	CCT	CORRECTED IOP	IOP	CCT	CORRECTED IOP	IOP	CCT	CORRECTED IOP
250427	62	F	CF CF	0.01	DENSE PSC+NS2+ CORTICAL	YES	12	527	13	12	540	13	12	532	13	12	524	13
250250	78	M	1/60	1.8	PSC+ NS2+ CORTICAL	YES	18	541	18	16	535	17	18	534	19	16	518	18
265281	58	F	3/60	1.3	PSC+ NS2 + CORTICAL	YES	10	547	10	10	540	11	14	536	15	10	530	11
259581	82	M	1/60	1.8	PSC+ NS 2 + CORTICAL	YES	16	540	17	14	530	15	16	538	17	18	510	21
259448	88	M	PL +VE ,PR accurate	0.016	SHMC	YES	14	567	13	10	545	10	12	540	13	10	526	11
268078	74	F	2/60	1.5	PSC+NS1-2	YES	16	534	17	14	537	15	14	542	14	12	536	13
241048	51	F	2/60	1.5	CENTRAL DENSE + PSC+ NS2+ CORTICAL	YES	20	545	20	16	541	16	14	544	14	12	540	13
262353	70	F	HM+	0.001	SMC	YES	16	549	16	12	544	12	12	546	12	12	542	12
259448	76	M	PL-VE	0.0013	NS4+CORTICAL	YES	16	547	16	18	542	18	16	544	16	14	544	14
262841	88	F	CF CF	0.01	PSC+NS2-3	YES	16	528	17	12	528	13	14	528	15	12	522	13
270403	80	F	CF CF	0.01	NS4	YES	10	545	10	12	543	12	14	545	14	12	540	13
270403	78	M	3/60	1.3	PSC+NS1-2	YES	20	544	20	20	539	21	20	539	21	20	530	21
271637	69	F	1/60	1.8	CENTRAL PSC+ NS 3 + CORTICAL	YES	14	546	14	12	536	13	10	531	11	10	530	11
254801	73	M	1/60	1.8	CENTRAL PSC+ NS 1-2+ CORTICAL	YES	12	542	12	8	539	9	8	520	10	8	512	10
271669	74	M	1/60	1.8	PSC+ NS 3 + CORTICAL	YES	14	548	14	12	532	13	12	530	13	12	524	13
264255	75	M	HM+	0.001	SHMC	YES	22	545	22	18	541	18	20	530	21	16	526	17
277757	70	F	PL +VE ,PR accurate	0.016	SMC	YES	16	556	15	12	538	13	12	564	11	12	518	14
181187	66	F	1/60	1.8	PSC+ NS1+2+ CORTICAL	YES	18	525	19	16	536	17	12	531	13	12	522	13
150721	66	M	2/60	1.5	NS-2+ CORTICAL	YES	16	540	17	16	535	17	10	531	11	12	520	14
216415	69	M	6/60	1	PSC+NS1+CORTICAL	YES	22	520	24	20	514	22	20	510	23	20	511	22
219802	56	M	1/60	1.8	PSC+NS1-2	YES	20	536	21	18	538	19	18	536	19	14	520	16
211078	58	F	3/60	1.3	CENTRAL PSC+ NS 2-3+ CORTICAL	YES	16	482	20	14	478	19	16	478	21	18	485	22
218331	82	F	2/60	1.5	CENTRAL PSC+ NS 1-2+ CORTICAL	YES	18	496	22	18	490	22	10	498	14	18	486	22
216003	61	M	2/60	1.5	PSC+ NS 2-3 + CORTICAL	YES	18	505	21	16	503	19	18	506	21	20	514	22
218610	52	M	6/24	0.6	NS1+CORTICAL	YES	20	510	23	18	512	20	20	511	22	20	520	22
566852	54	M	PL +VE ,PR accurate	0.016	SMC	YES	16	500	20	18	495	22	18	489	22	14	486	18
574349	60	F	CF CF	0.01	PSC+ NS1+2+ CORTICAL	YES	20	518	22	18	517	20	14	518	16	16	517	18
548642	72	F	1/60	1.8	NS-2+ CORTICAL	YES	22	524	23	18	528	19	22	525	23	22	520	24
204932	73	M	CF CF	0.01	NS3-4	YES	18	487	22	20	485	24	16	485	20	10	486	14
154868	75	M	CF CF	0.01	NS3-4+	YES	18	505	21	16	502	19	16	503	19	8	505	11
211078	67	M	2/60	1.5	CENTRAL DENSE PSC+ NS2-3+CORTICAL	YES	14	533	15	12	530	13	12	532	13	10	525	11
216415	60	F	1/60	1.8	NS 2+CORTICAL +PSC	YES	18	519	20	18	514	20	14	515	16	14	520	16
219802	74	M	CF CF	0.01	NS 3-4+CORTICAL+PSC	YES	16	475	21	18	480	23	16	478	21	16	476	21
211078	64	F	2/60	1.5	PSC+NS2+CORTICAL	YES	22	521	23	20	526	21	22	527	23	22	516	24
218331	65	F	1/60	1.8	PSC+NS2+CORTICAL	YES	20	508	23	18	509	21	20	510	23	16	508	19
216003	65	M	4/60	1.2	PSC+NS2+CORTICAL	YES	18	496	22	12	493	16	18	494	22	18	490	22
218610	63	M	HM+	0.001	SMC	YES	18	525	19	16	530	17	16	520	18	12	518	14
566852	79	M	6/36		PSC+NS1+CORTICAL	YES	14	547	14	14	541	14	20	530	21	16	526	17
574349	73	F	HM+		SMC	YES	14	550	14	12	544	12	14	541	14	12	534	13
548642	65	F	3/60		NS1 +CORTICAL	YES	13	527	14	16	531	17	12	531	13	12	522	13
549452	53	M	4/60		DENSE PSC+NS1-2	YES	12	531	13	16	534	17	10	541	10	12	544	12
550061	81	F	2/60		PSEUDOPHAKIA+PCO	YES	18	520	20	20	514	22	14	510	17	20	514	22
551947	79	M	PL+, PR Accurate		PSC+NS2+CORTICAL	YES	14	516	16	18	538	19	18	536	19	14	520	16
525800	61	M	1/60		PSC+NS2	YES	16	482	20	14	478	19	16	478	21	18	485	22
525930	64	F	6/36		PSC+NS1-2+CORTICAL	YES	14	496	18	18	490	22	10	498	14	18	486	22
525936	73	F	6/36		PSC+NS1-2+CORTICAL	YES	16	521	17	16	503	19	18	506	21	20	514	22
525950	75	M	HM+		NS3+CORTICAL	YES	14	510	17	18	512	20	20	511	22	20	520	22
511211	74	F	6/36		NS2-3+CORTICAL	YES	10	524	11	18	495	22	18	489	22	14	486	18
508780	62	F	PL+, PR Accurate		SMC	YES	16	518	18	18	519	20	14	518	16	16	517	18
502902	62	M	HM+		SMC	YES	12	527	13	18	528	19	22	525	23	22	520	24
497270	68	M	6/60		PSC+NS2	YES	14	490	18	20	484	24	16	485	20	10	486	14