A PROSPECTIVE CROSS-SECTIONAL STUDY OF CORRELATION OF OCULAR PSEUDOEXFOLIATION WITH SYSTEMIC VASCULAR DISEASES

By

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In
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I, ***Dr. Vaishnavi Patil,*** *hereby declare that this dissertation/thesis entitled "****A prospective cross-sectional study of correlation of ocular pseudoexfoliation with systemic vascular diseases"*** *is a bonafide and genuine research work carried out by me under the guidance of* ***Prof. (Dr.) Vallabha K*** ***MBBS, MS, DOMS*** *Professor, Department of Ophthalmology, B.L.D.E (DU)'s Shri B.M Patil Medical College, Hospitaland Research Centre, Vijayapura.*

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List of abbreviations

Abbreviations	Full expansion
PEX	Pseudoexfoliation
ECG	Electrocardiogram
LOX1	Lysyl oxidase 1
CLU	Clusterin
LOXL1	Lysyl oxidase-like 1
SNP	Single nucleotide protein
FBN1	Fibrillin 1
LTBP2	Latent TGF-beta binding proteins 2
MFAP2	Microfibril-associated protein 2
TGF-b1	Transforming growth factor b1
TGM2	Trasglutaminase 2
IL-6	Interleukin 6
IL-8	Interleukin 8
IOP	Intraocular pressure
OHT	Ocular hypertension
POAG	Primary open-angle glaucoma
XFG	Exfoliation glaucoma
CAD	Coronary artery disease
CRP	C reactive protein
hs-CRP	High-sensitivity C reactive protein
TNF-α	Tissue necrosis factor-alpha
ELISA	Enzyme-linked immunosorbent assay
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
VLDL	Very low-density lipoprotein
IHD	Ischemic heart disease
COPD	Chronic obstructive pulmonary disease
GLS	Global longitudinal strain
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
FBS	Fasting blood sugar
PPBS	Post-prandial blood sugar
SPSS	Statistical package for the social sciences
SD	Standard deviation
CVA	Cerebrovascular accidents
TG	Triglyceride

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Abstract

Background: Pseudoexfoliation syndrome [PEX] is characterized by a powdery substance in the anterior chamber, composed of various glycoproteins, which have an unclear origin. Its deposition is observed on the pupillary margin, lens zonules, and trabecular meshwork. Proteomic studies have identified numerous proteins in affected individuals, suggesting associations with systemic conditions like heart disease, stroke, and Alzheimer's disease. However, the systemic associations of PEX remain inconclusive, particularly in regions like southern India.

Materials and Methods: A cross-sectional study was conducted on 114 participants. Pseudoexfoliation was graded as mild, moderate and severe per a standard photographic grading. Systemic examinations included blood pressure measurements, electrocardiography, and blood investigations for serum lipid profile, fasting and postprandial blood sugar levels, and serum C-reactive protein levels. All the patients underwent small incision cataract surgery. Intraoperative complications and postoperative status were noted down.

Results: Thirty-eight patients (33.3%) had mild PEX, 44 (38.6%) had moderate PEX, and 32 (28.1%) had severe PEX. Hypertension was present in 54 participants (47.4%), diabetes in 21 (18.4%), coronary artery disease in 9 (7.9%), and cerebrovascular accidents in 3 (2.6%). The mean systolic blood pressure was 140.39 mmHg, and the mean diastolic blood pressure was 90.37 mmHg. Systolic blood pressure exceeded 140 mmHg in 29 participants (90.6%) with severe PEX, while diastolic blood pressure surpassed 90 mmHg in 26 (81.3%) participants with severe PEX, with a p-value of 0.001. Mean fasting and postprandial blood sugar levels were 103.80 ± 31.81 mg/dl and 131.72 ± 48.24 mg/dl, respectively. Electrocardiographic results indicated that 54 participants (47.37%) had abnormal ECGs, including rate, conduction,

ischemic, and structural defects. Of these, 13.2% had rate defects, 12.3% had conduction defects, 10.5% had ischemic changes, and 11.4% had structural defects.

Conclusion: This study highlights the significantly elevated parameters of systemic vascular diseases in PEX patients, like elevated blood pressure and more frequent cardiac abnormalities, emphasizing the need for comprehensive systemic evaluation and careful preoperative assessments for ocular complications

Introduction

"Pseudoexfoliation syndrome" was first documented by "John Gustaf Lindberg" almost a hundred years ago[1,2]. It is characterized by a 'dandruff-like' substance in the anterior chamber with a unique deposition pattern on the "anterior lens capsule, creating a double concentric ring pattern with a clear zone associated with an iris movement." PEX material is also observed at the pupillary margin, lens zonules, and trabecular meshwork, composed of various glycoproteins with an unclear origin, potentially deriving from the "iris, lens epithelium, ciliary body, or trabecular meshwork" [3]. It has a significant variation in prevalence across different geographical regions, ranging from 0% to 38%, even within the same population [4] and its prevalence increases with age [5]. Severe genes have been attributed to PEX, notably LOX1 and CLU genes. [6–9]

Proteomics studies have identified proteins such as "vitamin D binding protein," "apolipoprotein A4", "lysyl oxidase-like-1", and "complement C3" in the anterior segment tissues and fluids of individuals affected by PEX[10]. The protein composition of PEX syndrome was investigated using liquid chromatography and tandem mass spectrometry, identifying 66 proteins, including 13 novel constituents, with gene expression analysis and pathway studies implicating "extracellular matrix organization, elastic fiber formation, and the complement cascade," offering molecular insights into the disease's complexity and its associations with heart disease, stroke, and Alzheimer's disease [11,12]. Electron microscopic and ultrastructural examinations have demonstrated the presence of PEX materials in various visceral organs and extraocular sites, identifying them "adjacent to elastic and oxytalan fibers," with "positive staining for elastin and human amyloid P protein," resembling characteristics observed in ocular sites [3,13,14]. Moreover, there has been evidence of coronary artery

disease, hypertension, electrocardiogram abnormalities, dyslipidemia and elevated C-reactive protein in PEX patients. [15–21]

Substantial literature suggests a “positive association of PEX with ischemic heart disease and blood pressure.” However, some studies found no significant links, and many were limited by reliance on hospital health records for systemic disease assessment [19,22–24]. Few studies have been conducted on PEX and its systemic associations in India. Due to previous studies’ inconclusive and inconsistent results, further research is needed, especially in southern India. It may have significant public health and clinical implications, as slit-lamp examinations for PEX diagnosis could identify individuals at increased risk of diabetes, hyperlipidemia, hypertension, and cardiovascular abnormalities. This study aims to determine the correlation between the severity of ocular PEX and abnormalities of systemic vascular parameters, as well as the prevalence of PEX and its ocular manifestations.

Review of literature

Historical background

John Gustaf Lindberg (1884–1973) first documented exfoliation syndrome in his doctoral thesis a hundred years ago when he was doing a residency in ophthalmology. (1,2)

Motivation for his work is rooted in Theodor Axenfeld's observations (25), which highlighted the remarkably feeble response to standard mydriatics frequently observed in elderly eyes. Lindberg had reviewed articles by Axenfeld in which two forms of "age-related iris degenerations" were delineated. The "first type" was marked by "hyaline degeneration of the pupillary border," while the "second type" exhibited "autonomous pigmentary atrophy and depigmentation of the iris pigment epithelium." (2,25)

Lindberg also cited early observations by Fuch (1,26), who stated, "*In some eyes, I observed a strange change of the tissue behind the sphincter. At the pupillary border, it assumed a homogeneous hyaline character, which in part was also displayed by the septa penetrating the sphincter. (...) Owing to this transformation, the tissue has not only assumed an appearance resembling hyaline cartilage, but it has also increased in volume so that the sphincter is separated from the pigment layer as far as the pupillary border by a rather thick layer of tissue*."

Tarkkanen A (27) emphasizes Lindberg's pioneering work on "greyish flakes and fringes at the pupillary border and anterior lens capsule," which Lindberg observed "could coalesce into a membrane or circular disc." Lindberg noted age as a critical factor in the prevalence of these flakes, which are more common in senile cataracts and control patients aged 55 or older. Among Lindberg's subjects(1,27), including 60 chronic glaucoma patients, 50% had these flakes in the pupillary margin, as highlighted by Tarkkanen A.

Tarkkanen A (27) outlined various theories on the subject. Some authors proposed that uveal vascular changes, resembling a form of exudation, might be involved in exfoliation. Other implicated sources included the "iris pigment epithelium, aqueous humor, descemet membrane, zonule, lamina vitrea of the Bruch membrane, vitreous, and the lens capsule." Some hypothesized that "chemically altered aqueous humor could precipitate on the lens capsule." Moreover, it was theorized that "aqueous humor might have a degenerative impact on the lens capsule, eventually leading to exfoliation."

In 1957, Ashton suggested the ciliary epithelium as the primary site of involvement, referencing Dvorak-Theobald's (28) histologic examination, where she termed the condition "pseudocapsular exfoliation." She identified accumulations of "unknown material, deposits, mucopolysaccharides, and tyrosine on the anterior lens surface," introducing the term "pseudoexfoliation" to differentiate it from "true exfoliation," aiming to characterize the unique nature of the observed accumulations and their association with the anterior lens structures.

Elschnig documented "true exfoliation syndrome" (29), a rare eye condition, with an initial report focusing on two glassblower patients. Subsequently, Dvorak-Theobald(30) observed a decrease in the compelling need to differentiate "patients with true exfoliation of the lens capsule," as this condition has become uncommon.

Epidemiology

Patil et al. note that pseudoexfoliation syndrome, an age-related condition, demonstrates significant variations in prevalence across different geographical regions, ranging from 0% to 38%, even within the same population. (4) The reasons for these variations remain inadequately studied. Such differences might arise from genuine biological or ecological factors or be

influenced by variances in examination methods and diagnostic capabilities, as described in multiple studies. (31–36)

Forsius H's study reveals that pseudo-exfoliation syndrome prevalence, ranging from 5% to 20%, is significantly elevated in populations with Scandinavian, Northern European, and Mediterranean ancestry, significantly impacting Nordic and Eastern Mediterranean countries. In contrast, East Asian and Inuit populations, including Greenland Inuits, exhibit the lowest reported prevalence, potentially reaching zero. (33)On the other end of the spectrum, Faulkner, in 1971, noted that the prevalence of pseudo-exfoliation syndrome could be notably high, reaching up to 38% among Navajo Nation Indians. (37)

In Mitchell et al.'s Blue Mountains Eye Study (1999), "pseudoexfoliation was diagnosed in 2.3% of subjects, and its prevalence increased with age". (5) In a 2004 study in China by Young et al., pseudoexfoliation was found to be a "rare condition among Chinese individuals, with a prevalence rate of 0.4% observed in patients aged 60 or above", indicating its lower occurrence in this demographic group within the Chinese population. (31) As per Irvine's 1940 study, the historical incidence of pseudoexfoliation in India is reported at 8%, which Irvine attributes to examining exclusively elderly patients admitted for cataract extraction. (38)

According to a 1968 study by Sood et al., "the incidence of pseudoexfoliation in South India" is reported as 1.87% in all subjects over 50 years, increasing to 3.12% in those over 60 years, and reaching 9.62% among individuals over 70 years, suggesting an age-related rise in occurrence, particularly in older age groups. (34) According to a "hospital-based study" conducted in India in 2003, the "prevalence of pseudoexfoliation syndrome varies significantly, ranging from 1.87% to 13.5%". (39)

In 2015, Vijayalaxmi et al. conducted a study on the prevalence of pseudoexfoliation in Southern India, reporting a prevalence of 0.6% for patients with Pseudoexfoliation Syndrome (PXF) and noting an observed increase in PXF prevalence with advancing age. (40)

Genetics

In 2011, Schlötzer-Schrehardt mentioned that pseudoexfoliation syndrome is a complex, late-onset condition influenced by genetic and non-genetic factors. Although LOXL1 is a notable genetic risk factor, the specific causative variants remain unclear, implying potential contributions from additional genes or environmental factors in developing pseudoexfoliation syndrome. (6)

Thorleifsson et al. 2007 identified three LOXL1 gene variants “associated with a 2.5-fold increased risk” of pseudoexfoliation syndrome, forming a high-risk haplotype linked to a 700 times higher risk in carriers. (7) Chen et al. (2010) found a consistent association between the rs3825942 SNP in LOXL1 and exfoliation syndrome/glaucoma but no significant association with primary open-angle glaucoma across diverse populations. (8)

Krumbiegel et al. (2009) investigated genetic factors associated with pseudoexfoliation syndrome and glaucoma by examining six candidate genes in German cohorts. Only rs2279590 in the CLU gene was associated with pseudoexfoliation in Germans, highlighting potential ethnic differences in genetic susceptibility. “FBN1, LTBP2, MFAP2, TGF-b1, and TGM2” did not play a significant role in pseudo-exfoliation syndrome etiology in the German population. (9)

Proteomics of pseudoexfoliation

According to Morris et al. (2021), Pseudoexfoliation syndrome involves the accumulation of microfibrillar material in ocular structures, leading to pseudoexfoliation glaucoma (PEXG) and increased intraocular pressure. Proteomics studies have identified proteins such as "vitamin D binding protein," "apolipoprotein A4", "lysyl oxidase-like-1", and 'complement C3' in Pseudo-exfoliation-affected individuals' anterior segment tissues and fluids. The varying levels of these proteins across eye structures indicate their involvement. Both "genetic and environmental factors play a role in Pseudoexfoliation development," and ongoing research aims to unravel their impact on protein expression and function, contributing to understanding Pseudoexfoliation glaucoma's pathophysiology. (10)

In a study by Sharma et al. (2018), the protein composition of pseudoexfoliation syndrome, an age-related ocular disease with systemic implications, was investigated. Using liquid chromatography and tandem mass spectrometry, 66 proteins within pseudoexfoliation material, including 13 novel constituents, were identified, offering insights into the disease's complexity. Gene expression analysis suggested contributions from the lens epithelium and aqueous humor to pseudoexfoliation material. Pathway and network analyses implicated "extracellular matrix organization," "elastic fiber formation," and the "complement cascade," with fibronectin playing a central role. The findings provided molecular perspectives on pseudoexfoliation syndrome's associations with heart disease, stroke, and Alzheimer's disease, advancing our understanding of its pathophysiology. (11)

Zenkel et al. 2010 explored proinflammatory cytokines' role in PEX syndrome/glaucoma, finding a threefold increase in "IL-6 and IL-8" during "early stages." Late-stage PEX/glaucoma showed no significant differences from controls. The study implies

that stress-induced inflammation contributes to the fibrotic matrix in PEX syndrome/glaucoma initiation. (12)

Ocular manifestations

In 2006, “Schlotzer-Schrehardt U and Naumann GO” elucidated the “ocular features of pseudoexfoliation syndrome,” emphasizing “the deposition of fibrillar material on structures in contact with the aqueous humor,” this substance is visually evident during slit lamp examinations, presenting as a “dandruff-like substance in the anterior chamber.” The unique deposition pattern on “the anterior lens capsule creates a double concentric ring pattern with a clear zone associated with iris movement.” Pseudoexfoliation material is also observed at the “pupillary margin, lens zonules, and trabecular meshwork,” composed of various glycoproteins with an unclear origin, potentially deriving from the “iris, lens epithelium, ciliary body, or trabecular meshwork.” (3)

Figure 1: Pseudoexfoliation with anterior capsular delamination. Image credit: Allingham et al. (41)

According to Tomczyk-Socha et al. (2023), alterations in the iris involving the pupillary sphincter muscle are a characteristic feature of pseudoexfoliation syndrome. The manifestation of iris transillumination, often described as a moth-eaten peripupillary iris appearance, results from iris pigment epithelium abrasion caused by pupil movements. Acting like sandpaper on the iris, this material on the lens capsule releases a significant amount of pigment, leading to hyperpigmentation in the filtration angle and the "formation of pigment deposits on the iris surface." (42) Ritch, in 2018, mentioned that "pseudoexfoliative material and pigment precipitates may also be observed on the corneal endothelium," often resembling a "Krukenberg spindle." (43)

Tomczyk-Socha et al. also mention that identifying pseudoexfoliation syndrome in its initial phases poses a challenge. However, suspicion arises with a "uniform, dull appearance of the anterior lens capsule, resembling a clouded glass window," mainly if observed unilaterally. As pseudoexfoliation advances, delicate radial striations develop from the central disc, becoming more noticeable in low-light conditions. "The transparent zone between the central part and the peripheral ring" becomes apparent "only when the exfoliating material on the lens thickens." (42)

As per Schlotzer-Schrehardt U and Naumann GO (2006), no diagnostic procedures currently exist to confirm pseudoexfoliation syndrome other than "electron microscopy," which can unveil "the characteristic material in the anterior segment." (3) According to Sampaolesi, Zarate, and Croxato (1988), gonioscopy in patients with pseudoexfoliation syndrome may reveal the Sampaolesi line's characteristic, indicating intense and inhomogeneous trabecular meshwork pigmentation. (44)

As outlined by Tomczyk-Socha et al., pseudoexfoliation syndrome typically involves a "reduction in endothelial cell count and an increase in central corneal thickness."

These changes may expedite disruptions in endothelial cell homeostasis, potentially leading to corneal decompensation, opacity, and edema. Moreover, individuals with pseudoexfoliation syndrome "have a heightened postoperative incidence of ocular edema following cataract surgery." (42)

According to Detorakis et al. (2021) and Tomczyk-Socha et al. (2023), periocular changes in pseudoexfoliation syndrome encompass eyelid laxity, conjunctival chalasis, tear film abnormalities, orbital fat atrophy (particularly following the use of prostaglandin analogs), deficient orbital vascular supply, and biomechanical changes in the eyeball and optic nerve. (42,45)

Tomczyk-Socha et al. extensively discussed the intraoperative and postoperative consequences of pseudoexfoliation. Zonular weakness in PXF significantly elevates the risk of "intraoperative complications, including zonule rupture, posterior capsule rupture, vitreous body transition to the anterior segment, and the sinking of cataract masses into the vitreous chamber." Postoperatively, potential complications involve "chronic inflammation," "lens displacement," "lens subluxation," "posterior lens capsule opacification," "fibrosis," and "tightening of the lens capsule." It is noteworthy that diagnosing PXF in individuals who have undergone cataract extraction can be challenging, mainly when characteristic symptoms are absent on the "anterior lens capsule removed during the procedure," resulting in a considerable amount of undiagnosed cases, especially "in the absence of distinctive symptoms on the lens capsule." (42)

Pseudoexfoliation syndrome and secondary glaucoma

According to Irkec (2015) and Tomczyk-Socha et al. (2023), pseudo-exfoliation syndrome is the most prevalent identifiable cause of secondary glaucoma globally. "It is estimated that up to half of individuals with pseudoexfoliation syndrome will develop glaucoma at some point

in their lives." Those with pseudoexfoliation syndrome face a significantly elevated risk, approximately "6 to 10 times higher than the general healthy population," of developing glaucoma. Notably, the increased risk for elevated intraocular pressure and subsequent glaucoma often becomes apparent shortly after the clinical onset of pseudoexfoliation syndrome. (42,46)

In the Blue Mountains Eye Study, Mitchell et al. (1999) aimed to quantify the relationship between pseudoexfoliation and open-angle glaucoma, ocular hypertension (OHT), and intraocular pressure (IOP) in an older population. "Glaucomatous damage was present in 14.2% of eyes with pseudoexfoliation," indicating a solid association "independent of other glaucoma risk factors, including IOP." Despite a "low population-attributable risk from pseudoexfoliation (2.7%), ocular hypertension was more prevalent in eyes with pseudoexfoliation," highlighting the significant connection between pseudoexfoliation and glaucoma. (5)

Citing Ariga, Nivean, and Utkarsha (2013), pseudoexfoliative material obstructs trabecular meshwork spaces, causing pigment accumulation and hindering "aqueous humor outflow, leading to persistent intraocular pressure elevation and pseudoexfoliation glaucoma." In unilateral cases," the affected eye exhibits "approximately 2 mm Hg higher IOP than the non-exfoliative fellow eye, highlighting pseudoexfoliation's impact on glaucoma development. (47)

Ariga et al. (2013) and Konstas (1997) mention that pseudoexfoliation syndrome induces vascular degeneration, chronic disruption of the aqueous humor–blood barrier, and compromised ocular blood flow. Pupil dilation in pseudoexfoliation syndrome releases "dispersed pigment from the iris, obstructing the filtration angle and causing a significant elevation in IOP." Reevaluation of IOP in individuals with pseudoexfoliation syndrome after

pupil dilation becomes crucial to consider the potential impact of this process on IOP levels. (47,48)

Ariga et al. additionally notes that the progression of glaucoma associated with exfoliation syndrome exhibits greater severity than primary open-angle glaucoma (POAG). This indicates that individuals with exfoliation syndrome may undergo a more challenging and potentially aggressive disease progression than those with POAG (Ariga et al., 2013). (47)

The study by Konstas et al. (48) revealed that "the baseline intraocular pressure (IOP) was higher in patients with exfoliation glaucoma (XFG) compared to those with primary open-angle glaucoma (POAG)." This observation aligns with similar findings reported by Tezel and Tezel (49,50). Furthermore, Teus et al.(51) demonstrated that "among untreated patients, a higher level of IOP was associated with a more significant loss of visual field." These consistent findings across multiple studies emphasize the importance of baseline IOP levels in understanding the differences between XFG and POAG and their potential implications for visual field loss.

Systemic association

Schlötzer-Schrehardt, in his 1992 reports, provides electron microscopic evidence demonstrating "the presence of pseudoexfoliation material in various visceral organs." (13)

In 1992, Streeten conducted an ultrastructural examination of tissues from a deceased glaucoma patient with bilateral ocular pseudoexfoliation, revealing the presence of pseudoexfoliative material aggregates not only in conventional intraocular locations but also in extraneous organs "such as the lung, heart, liver, and gallbladder." These aggregates, often located "adjacent to elastic and oxytalan fibers," exhibited positive staining for "elastin and human amyloid P protein," resembling characteristics observed in ocular sites. (14)

In a 2009 cross-sectional study by Andrikopoulos et al. investigating cataract patients with pseudoexfoliation syndrome, 2140 individuals undergoing cataract surgery at the University Hospital of Patras, Greece, were examined. Focused on senile cataracts, participants underwent thorough ophthalmological examinations and CAD evaluations. Pseudoexfoliation syndrome exhibited a 27.9% prevalence, increasing with age. Within this group, 22.1% had glaucoma, compared to 2.5% in the non-pseudoexfoliation group. Notably, pseudoexfoliation syndrome "was positively associated with CAD risk in those aged 50 or older." The study concluded that pseudoexfoliation syndrome significantly elevates the risk for both glaucoma and CAD.(15)

In a study by Mocan et al. (2011) involving 33 pseudoexfoliation syndrome subjects and 23 controls, serum CRP levels, indicative of inflammation, were measured using a nephelometric assay. The mean serum CRP level in "subjects with pseudoexfoliation did not significantly differ from healthy subjects." No significant differences were observed in age, gender ratio, and serum CRP concentrations among pseudoexfoliation syndrome, pseudoexfoliation glaucoma, and controls, suggesting limited local and subclinical inflammatory reactions in tissues associated with pseudoexfoliation. (16)

In a 2013 study by Gonen, 49 pseudoexfoliation syndrome patients and 42 controls were assessed using Doppler ultrasonography. Significant associations were found between pseudoexfoliation syndrome and renal artery stenosis, with increased abdominal aorta velocities. Hypertension was common in pseudoexfoliation patients with renal artery stenosis, suggesting a potential link between the syndrome and aortic involvement. (17)

Sorkhabi et al. 2013 conducted a study examining "high-sensitivity C-reactive protein (hs-CRP) and Tumor Necrosis Factor-alpha (TNF-α) levels in the blood serum of pseudoexfoliation syndrome (PEX) individuals." Using enzyme-linked immunosorbent assay

(ELISA) with 30 PEX cases and 30 matched controls, the research revealed significantly higher hs-CRP and TNF-α levels in PEX patients, suggesting "inflammation and peripheral endothelial dysfunction may contribute to the risk of systemic and ocular manifestations in pseudoexfoliation syndrome." (18)

In 2017, Vardhan et al.'s study, comprising 930 pseudoexfoliations (PEX) patients and 476 controls, provided crucial insights into cardiovascular implications. The study reveals a clinically significant "4.0 mm Hg increase in systolic blood pressure and a 1.64 odds ratio" for ECG abnormalities in PEX. The comprehensive analysis finds no associations with blood glucose, serum cholesterol, or homocysteine, offering clinicians valuable information for assessing cardiovascular risk and enhancing patient care. (19)

Led by Kurtul B in 2017, the investigation aimed to uncover the link between pseudoexfoliation (PEX) syndrome and serum lipid levels, focusing on its association with systemic vascular disorders. The study categorized participants into three groups: 52 with PEX syndrome (group 1), 20 with PEX glaucoma (group 2), and 47 controls without PEX (group 3). A biochemical analyzer assessed "fasting serum total cholesterol," "high-density lipoprotein (HDL)," "low-density lipoprotein (LDL)," and "triglyceride levels." The findings revealed "significantly higher mean LDL values in groups 1 and 2 than group 3", suggesting a significant association between elevated LDL values and PEX. (20)

The "prospective cross-sectional study" conducted by Vikram Chellakumar, Rashmi Priyanka, and Balakrishnan M in 2019 aimed to explore the prevalence of cardiovascular diseases associated with pseudoexfoliation syndrome. The findings revealed "that more than 60% of pseudoexfoliation patients had hypertension, but no statistically significant association with other cardiovascular conditions, such as angina, myocardial infarction, and cerebrovascular accidents," was observed. (21)

Published in August 2019, the study by Scharfenberg et al. explored systemic comorbidities in pseudoexfoliation syndrome. They analyzed 325 pseudoexfoliation–positive and 911 pseudoexfoliation–negative patients over 50 years undergoing ophthalmological operations, and the research was adjusted for age and gender. Pseudoexfoliation–positive patients exhibited increased odds ratios for respiratory, cardiac, vascular, and urogenital conditions. Nominal significance was noted for renal and psychiatric comorbidities. While no substantial associations were found for hernias and varicose veins, “higher rates of cardiac valve disorders and benign prostate hyperplasia were observed among pseudoexfoliation–positive individuals.” These findings imply a potential link between pseudoexfoliation and specific systemic conditions, warranting further exploration and histological studies. (23)

In 2020, Pooja H V, H T Venkate Gowda, and Subhash Chandra studied the connection between systemic disorders and pseudoexfoliative syndrome. Enrolling 67 patients aged 50-80 with pseudoexfoliative cataracts, they discovered that “25.37% had Diabetes mellitus, 10 had hypertension, 2 had IHD, and one had COPD”. The results underscore a significant association between pseudoexfoliation and diabetes mellitus. (22)

In 2020, Ugnė Rumelaitienė and colleagues conducted a study investigating “the 10-year incidence of pseudoexfoliation syndrome (PEX) in a population-based follow-up”. The research aimed to establish a connection between PEX and vascular diseases, exploring potential risk factors. Over the decade, “the prevalence of PEX increased from 10.3% to 34.2%”. The PEX group displayed “higher rates of ischemic heart disease (IHD) and IHD combined with stroke.” The study found a significantly elevated risk of PEX among individuals with IHD, and this risk was even higher in those with both IHD and stroke, suggesting a potential association between pseudoexfoliation syndrome and cardiovascular conditions. (24)

In a 2021 study by Çerik et al., which assessed 29 asymptomatic pseudoexfoliation syndrome (PEX) patients, speckle-tracking echocardiography revealed significantly lower global longitudinal strain (GLS) than healthy volunteers. While standard echocardiographic parameters showed marginal differences, the study suggests that GLS, indicating subclinical myocardial dysfunction, can serve as an independent predictor for PEX syndrome, emphasizing the need for cardiac function monitoring in PEX patients. (52)

In a 2022 prospective case-control study by Okutucu and Arpa, serum levels of semaphorin 3A and interleukin six were evaluated in 70 participants, including 30 with pseudoexfoliation syndrome and 40 controls. The pseudoexfoliation syndrome group exhibited statistically “higher IL-6 levels and lower Sema3A levels than controls”. The findings suggest a potential role for these molecules in the “systemic manifestations of pseudoexfoliation syndrome, implicating inflammation, atherosclerosis, heart arrhythmia, and Alzheimer’s disease in the syndrome’s pathophysiology.” (52)

Materials and methods

A Cross-sectional study was carried out at the Department of Ophthalmology in Shri B.M. Patil Medical College, Hospital, and Research Centre from August 2022 to January 2024, spanning eighteen months.

Ethical Considerations:

The study aimed to investigate the correlation between ocular pseudoexfoliation and systemic vascular diseases and identify the prevalence and ocular manifestations of pseudoexfoliation syndrome. The research adhered to the principles outlined in "the Declaration of Helsinki" (53) and received approval from the institutional ethical committee of BLDE (Deemed to be University) vide order number BLDE (DU)/IEC/687/2022-23. Before participation, all individuals provided written and informed consent, having been thoroughly briefed on the potential implications of the study.

Inclusion and exclusion criteria:

- **Inclusion Criteria:** Individuals aged over 40 years with ocular pseudoexfoliation.
- **Exclusion Criteria:**
    1. Individuals who have had previous intraocular surgery.
    2. Those with a history of trauma or uveitis.
    3. Individuals with significant corneal opacities that obscure anterior segment structures.
    4. Individuals with any ocular pathology that could result in secondary glaucoma.

Sample size:

The study aimed to achieve a sample size of 114 participants with a 95% confidence level with a 5% absolute precision, guided by the estimated prevalence of Pseudoexfoliation Syndrome in India(19). A thorough screening of 6,120 patients over eighteen months revealed 216 individuals with ocular pseudoexfoliation. Following the application of predetermined exclusion criteria, 102 individuals were excluded, resulting in a final cohort of 114 participants who satisfied the inclusion criteria and were included in the study.

Method of data collection

All patients attending the Ophthalmology outpatient and inpatient departments of Shri B.M. Patil Medical College, Hospital, and Research Centre for eighteen months underwent screening for pseudoexfoliation as part of the study.

A comprehensive patient history was gathered, covering aspects such as trauma and prior intraocular surgeries. Special attention was given to any significant history of past illnesses, including hypertension, diabetes, coronary artery disease and stroke. Best corrective visual acuity was evaluated using a Snellen chart, and subjective refraction was conducted whenever feasible. Following this, an extensive slit lamp examination (AIA – 11 – 5S – L; Appasamy Associates, Chennai, India) was done after diagnostic mydriasis with one drop of 1% tropicamide. It was confirmed that the diagnosis involved identifying the characteristic greyish-white exfoliation material on the anterior capsular surface of the lens, which could manifest in various forms, such as a complete or partial peripheral band and a central shield. Additionally, its presence might extend to other areas in the anterior chamber or be evident as pre-capsular frosting or haze.

All participants were graded into three groups [Mild, moderate, severe] as per the standard slit-lamp photographic grading explained by Aoki T et al. (54)

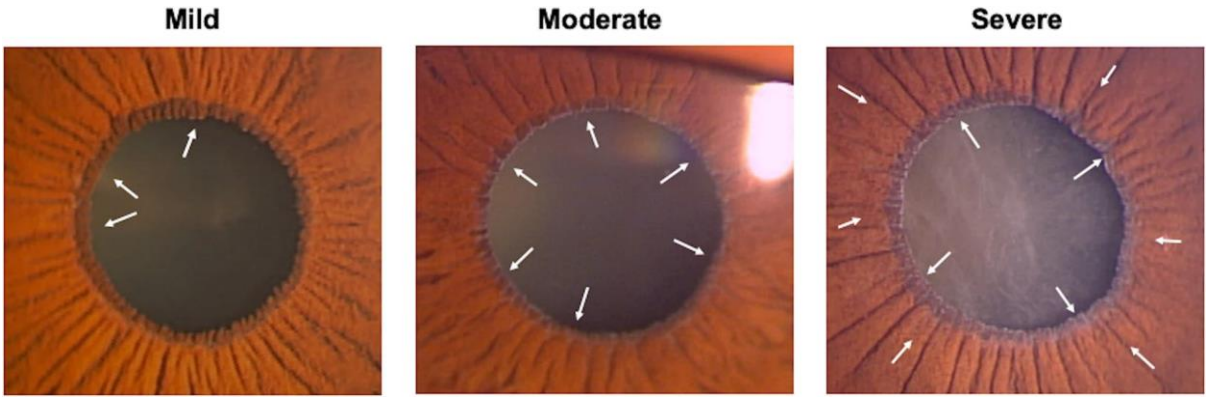


Figure 2: Grading of PEX into mild, moderate and severe.

Image courtesy Aoki T et al. (54)

Intraocular pressure was measured using a Goldmann applanation tonometer (AATM 5001; Appasamy Associates, Chennai, India). Gonioscopy was performed with a four-mirror goniolens (MIPL/14; Opticlear ophthalmic lenses, New Delhi, India), and fundus examination was carried out using binocular indirect ophthalmoscopy (AIO – 7; Appasamy Associates, Chennai, India).

A detailed, relevant systemic examination was performed. Blood pressure was measured for all enrolled subjects. Blood pressure was measured with a well-calibrated mercury sphygmomanometer in the left arm in a supine position. The starting of the first Korotkoff sound was taken as systolic blood pressure (SBP), and the ending of the fourth Korotkoff sound was considered diastolic blood pressure (DBP). Blood pressure was measured three times at an interval of one hour, and an average of three was taken. Twelve-lead electrocardiography (CARDIART 6208, BPL, Bengaluru, India) was performed, and the electrocardiogram interpretations were categorized into five groups. [TABLE 1]

Table 1: Group distribution according to electrocardiogram findings

Group	Electrocardiogram findings
1	Normal
2	Rate defects
3	Conduction defects
4	Ischemic defects
5	Structural defects

Blood investigations included serum lipid profile, fasting and postprandial blood sugar levels, and serum C-reactive protein levels, estimated using an automated analyzer (VITROS 5.1FS, Ortho-Clinical Diagnostics Inc., Raritan, NJ, USA). A plain bulb was used for lipid profile and C-reactive protein, and a grey bulb containing sodium fluoride was used for fasting and postprandial blood sugar levels. Early morning fasting blood samples were collected to measure fasting blood sugar (FBS) levels, serum low-density lipoprotein (LDL), serum very low-density lipoprotein (VLDL), serum triglyceride (TG), serum cholesterol and serum C-reactive protein (CRP) levels. A postprandial blood sugar (PPBS) level sample was collected two hours after breakfast.

Table 2: Normal reference levels considered for blood investigations

Investigations	Reference value
Fasting blood sugar	< 125 mg/dl
Postprandial blood sugar	< 200 mg/dl
Serum Low-density lipoprotein	< 130 mg/dl
Serum High-density lipoprotein	> 60 mg/dl
Serum Cholesterol	< 200 mg/dl
Serum Triglyceride	< 150 mg/dl
Serum C-reactive protien	< 10 mg/dl

All patients underwent small incision cataract surgery with intraocular lens implantation wherever possible. Preoperatively, 1% tropicamide eye drops were instilled for pupillary dilation along with Flurbiprofen 0.03% eye drops for pupillary stabilization. The intraoperative and postoperative course was recorded for every patient.

Statistical analysis:

With the expected prevalence of Pseudoexfoliation Syndrome (PEX) in India ranging from 1.87% to 13.5% (19), the study enrolled a sample size of 114 patients, aiming for a 95% confidence level and a 5% absolute precision. The formula used for determining the sample size was:

$$n = \frac{z^2 \times p \times q}{d^2}$$

Where:

- n is the desired sample size (114 in this case).
- z is the Z statistic at the α level of significance.
- d represents the absolute error (5% absolute precision).
- p is the proportion rate.
- q is calculated as $(100 - p)$

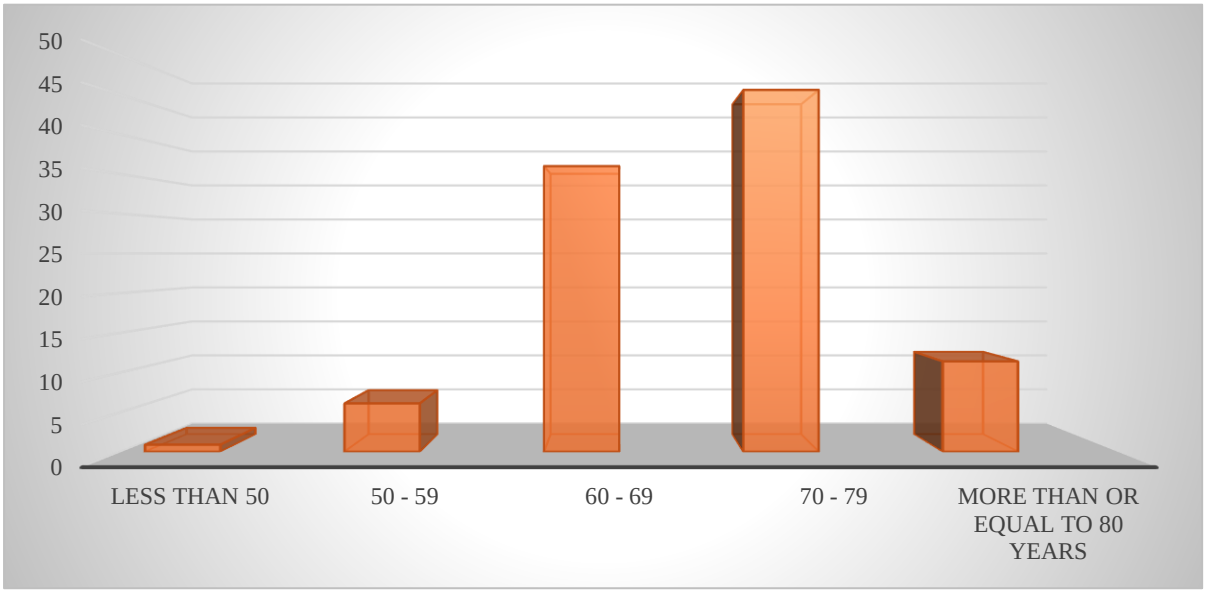
All data was tabulated in the master chart using a Microsoft Excel sheet (Office 365 Suite, Microsoft, Redmond, WA), and statistical analysis was conducted using SPSS Statistics Version 20 (IBM Corp., Armonk, NY). The results are expressed as Mean (Median) ± SD, counts, and percentages and represented using diagrams. The association of blood sugar levels, blood pressure, ECG, Lipid profile, and CRP with a grade of PEX is analyzed using the Chi-square test. At the same time, correlation coefficients are calculated for continuous variables. A significance level of $p < 0.05$ is deemed statistically significant. All statistical tests are two-tailed.

Results

A total of 6,120 patients were screened over 18 months, and 216 individuals were identified with ocular pseudoexfoliation. After applying predetermined exclusion criteria, 102 individuals were excluded, resulting in a final cohort of 114 participants. So, the prevalence of pseudoexfoliation in this region of Karnataka is 3.52%.

Table 3: Age distribution of the participants

Age group	Frequency(n)	Percentage (%)
Less than 50	1	0.90
50 - 59	7	6.10
60 - 69	41	36.00
70 - 79	52	45.60
More than or equal to 80 years	13	11.40
Total	114	100.0



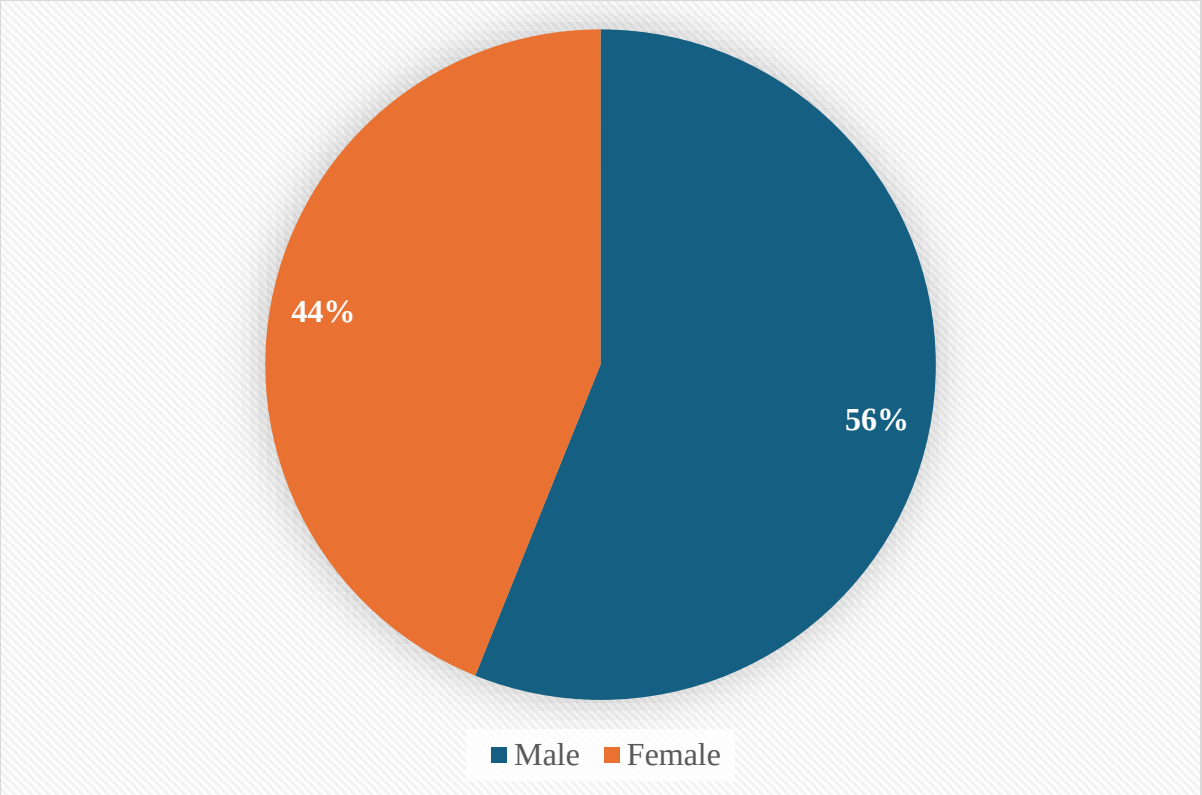
Graph 1: Bar graph showing the percentage distribution of ages among the participants

Among the 114 participants, the average age is 68.95 years (± 8.08 years). The age distribution is as follows: 52 (45.6%) participants are aged 70 to 79 years, 41 (36%) are 60 to 69 years,

13 (11.4%) are over 80 years, 7 (6.1%) are aged 50 to 59 years, and only 1 (0.9%) participant is under 40. [Table 3] [Graph 1]

Table 4: Gender distribution among the participants

Gender	Frequency(n)	Percentage (%)
Male	64	56.1
Female	50	43.9
Total	114	100.0

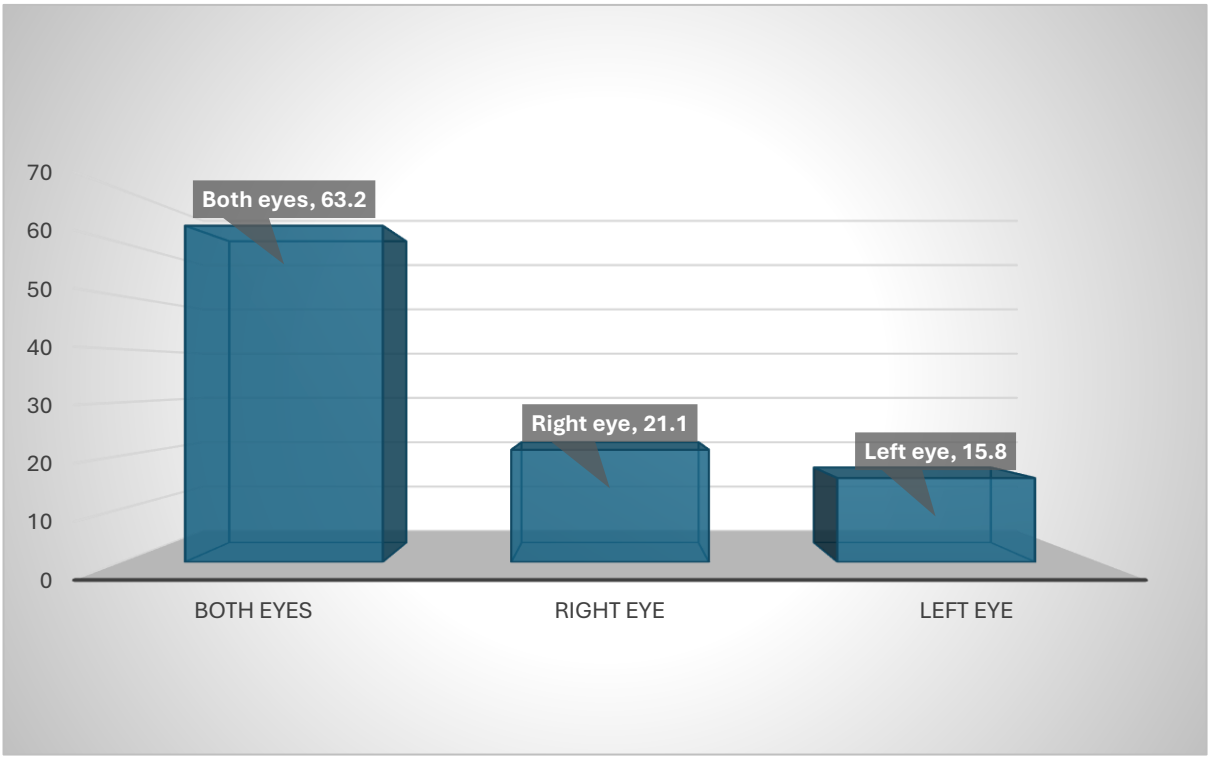


Graph 2: Pie chart showing the distribution of gender among the participants

Out of the 114 participants, there was a notable male predominance, with 64 (56%) males and 50 (44%) females. [Table 4] [Graph 2]

Table 5: Distribution of Pseudoexfoliation in the eyes of the participants

Eye considered	Frequency(n)	Percentage (%)
Both eyes	72	63.2
Right eye	24	21.1
Left eye	18	15.8
Total	114	100.0

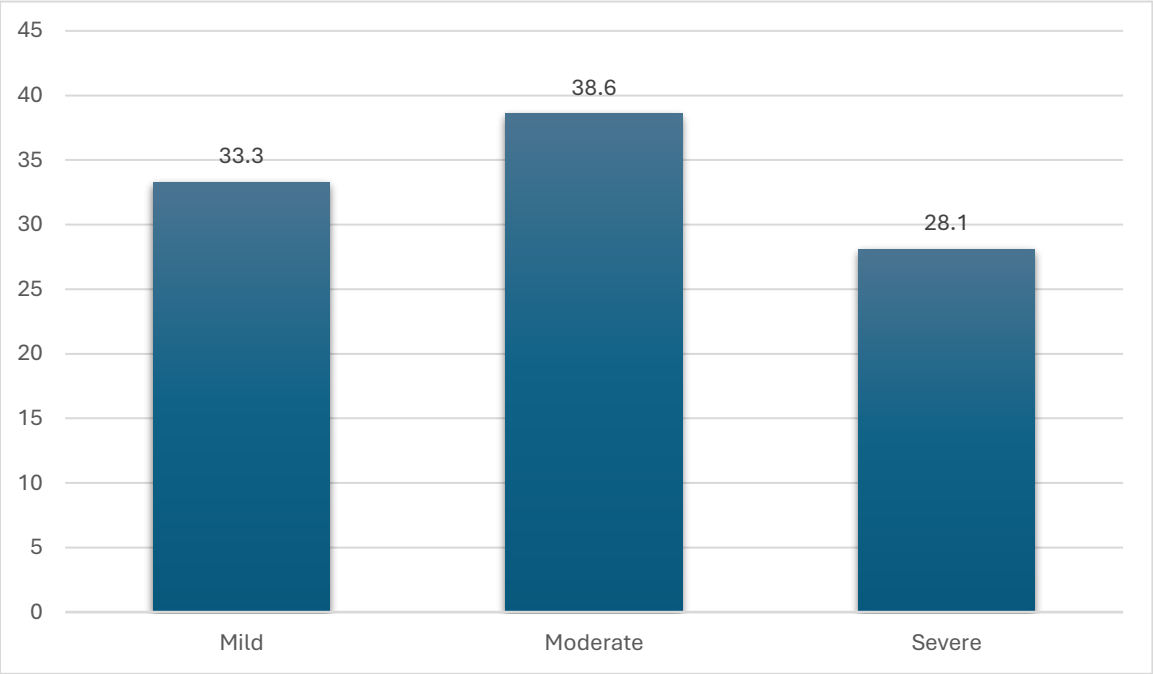


Graph 3: Bar graph showing the distribution of PEX in eyes of the participants

Out of the 114 participants, 72 (63.2%) had bilateral pseudoexfoliation, while 24 (21.1%) had pseudoexfoliation in the Right eye and 18 (15.8%) in the left eye. [Table 5] [Graph 3]

Table 6: Grades of pseudoexfoliation observed among the participants

Grading of PEX	Frequency(n)	Percentage (%)
Mild	38	33.3
Moderate	44	38.6
Severe	32	28.1
Total	114	100.0

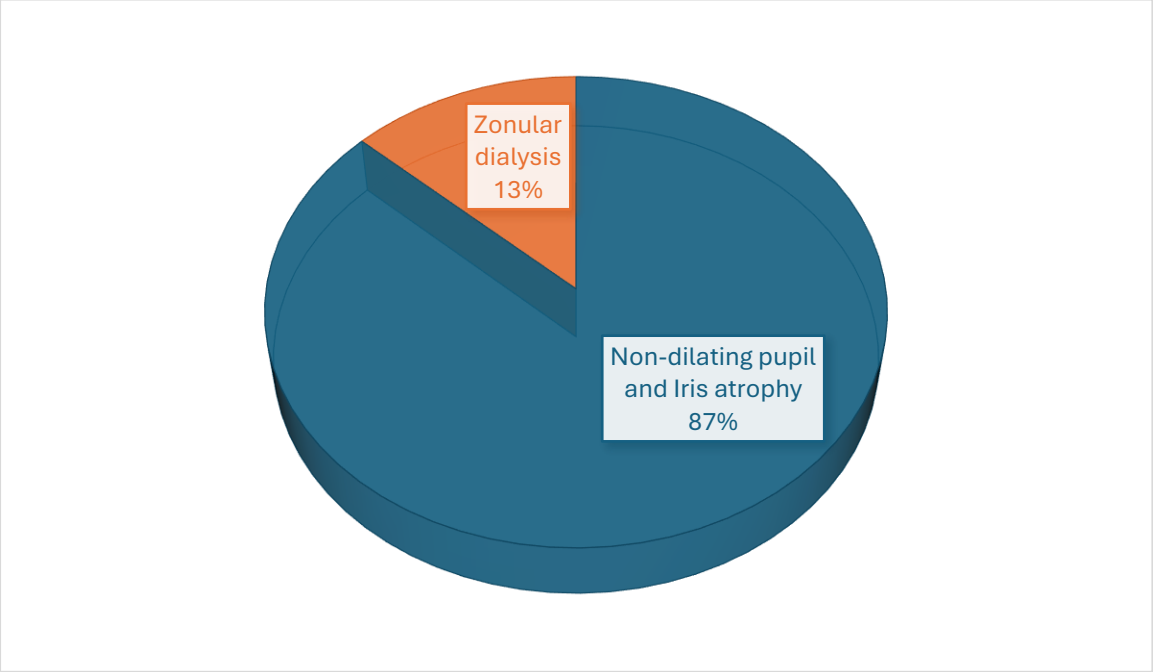


Graph 4: Bar graph showing the distribution of PEX as per severity grades.

Of 114 cases, 38 (33.3%) had mild, 44 (38.6%) had moderate, and 32 (28.1%) had severe PEX. This distribution indicates moderate PEX was the most common grade observed, followed by mild and severe cases. [Table 6] [Graph 4]

Table *7*: Ocular complications of pseudoexfoliation.

Complications	Frequency(n)	Percentage (%)
Non-dilating pupil and Iris atrophy	99	86.8
Zonular dialysis	15	13.2
Total	114	100.0

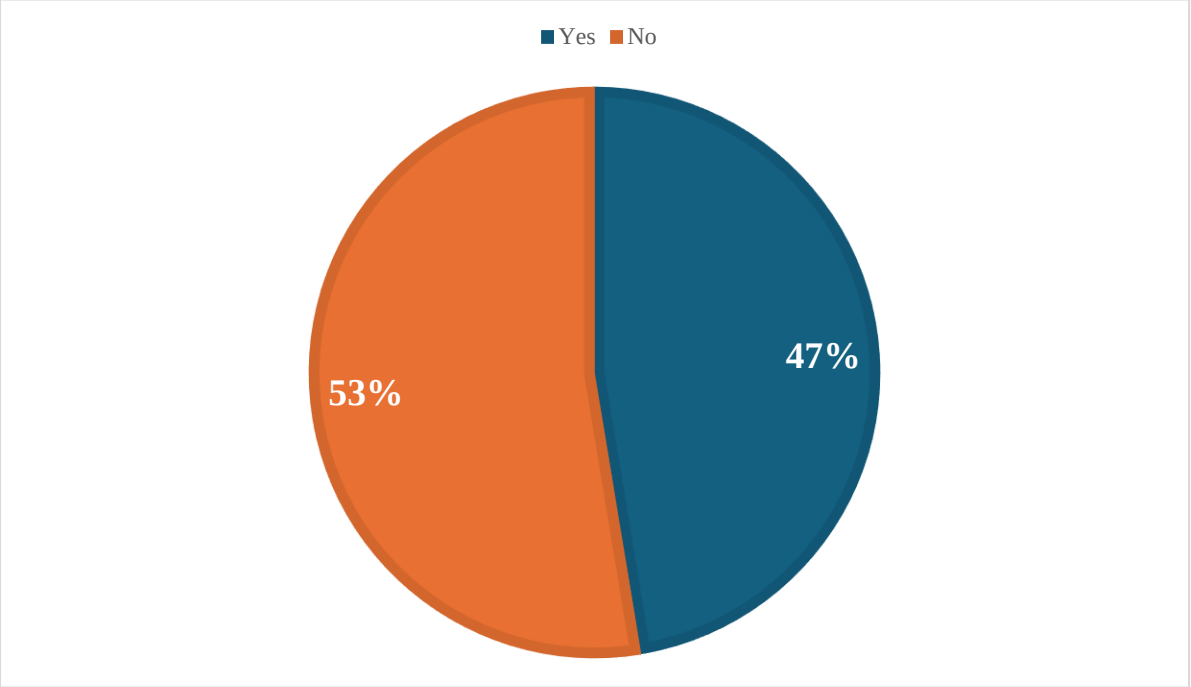


Graph 5: Pie chart showing ocular complications of pseudoexfoliation.

In this study involving 114 participants, a significant number displayed specific ocular conditions. The majority, 99 participants (86.8%), were observed to have non-dilating pupils and atrophic patches on the iris. Additionally, 15 participants (13.2%) were found to have zonular dialysis. [Table 7] [Graph 5]

Table 8: Distribution of hypertension among PEX patients

Hypertensive	Frequency(n)	Percentage (%)
Yes	54	47.4
No	60	52.6
Total	114	100.0

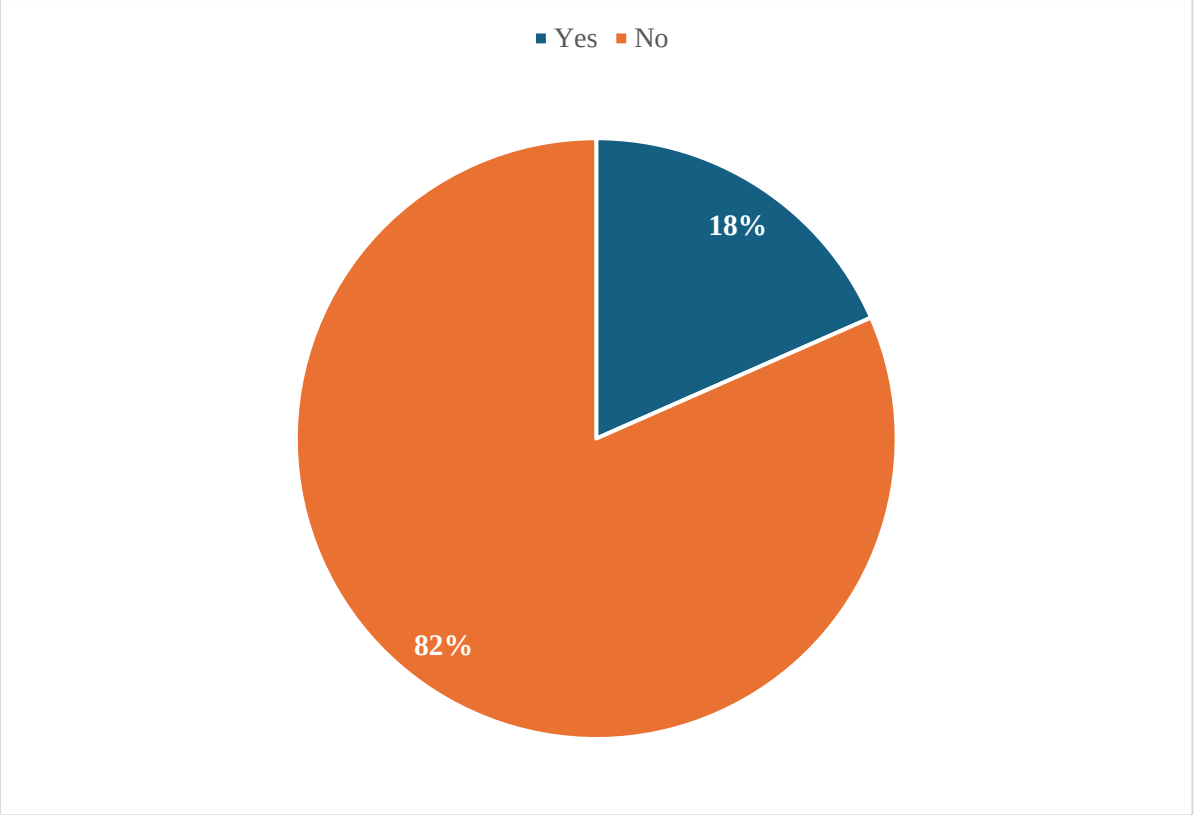


Graph 6: Piechart showing the percentage distribution of hypertension among PEX patients

Out of 114 patients in the study, 54 (47.4%) were known to have hypertension and were on anti-hypertensive medications, while 60 (52.6%) were not known to have hypertension. [Table 8] [Graph 6]

Table 9: Distribution of diabetes among PEX patients

Diabetes	Frequency(n)	Percentage (%)
Yes	21	18.4
No	93	81.6
Total	114	100.0

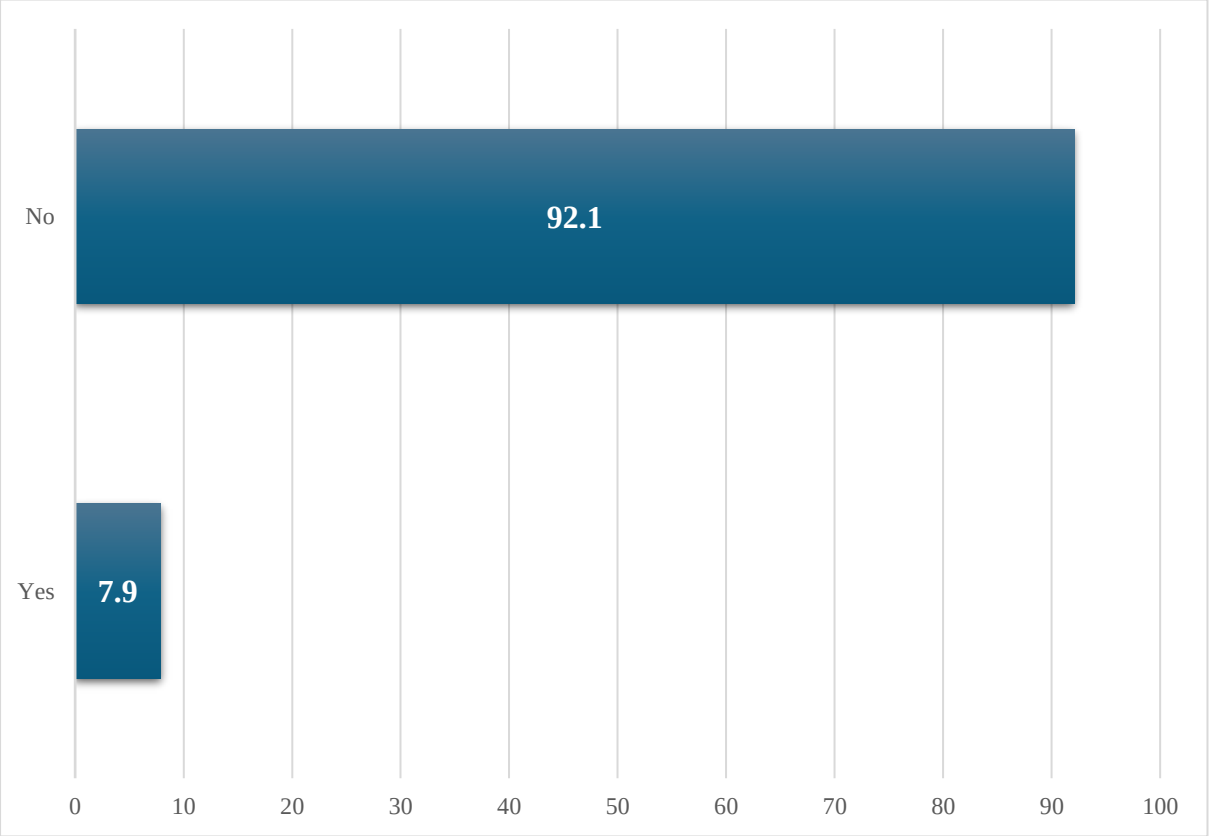


Graph 7: Piechart showing the percentage distribution of diabetes among PEX patients

Among our study participants, we had fewer cases of diabetes mellitus. Out of 114 patients, 21 (18.4%) had diabetes, and all were taking oral hypoglycemic medications. [Table 9] [Graph 7]

Table 10: Distribution of Coronary artery disease among PEX patients

Coronary artery disease	Frequency(n)	Percentage (%)
Yes	9	7.9
No	105	92.1
Total	114	100.0

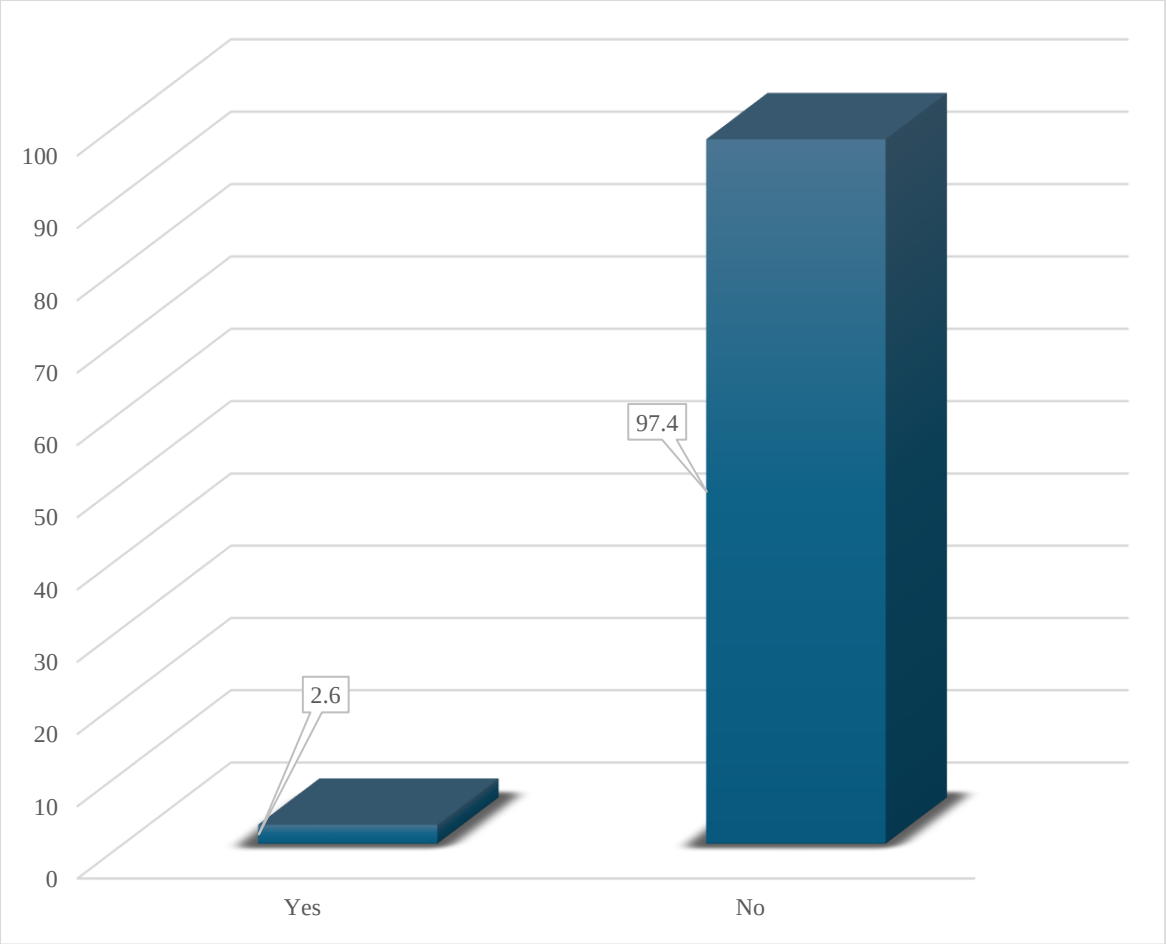


Graph 8: Bar graph showing the distribution of coronary artery disease among PEX patients

Among all participants, only nine individuals (7.9%) had previously been diagnosed with coronary artery disease and were receiving medication. In contrast, the vast majority, 105 participants (92.1%), were unaware of their heart health or the presence of coronary artery disease. [Table 10] [Graph 8]

Table 11: Distribution of history of stroke among PEX patients

Stroke	Frequency(n)	Percentage (%)
Yes	3	2.6
No	111	97.4
Total	114	100.0

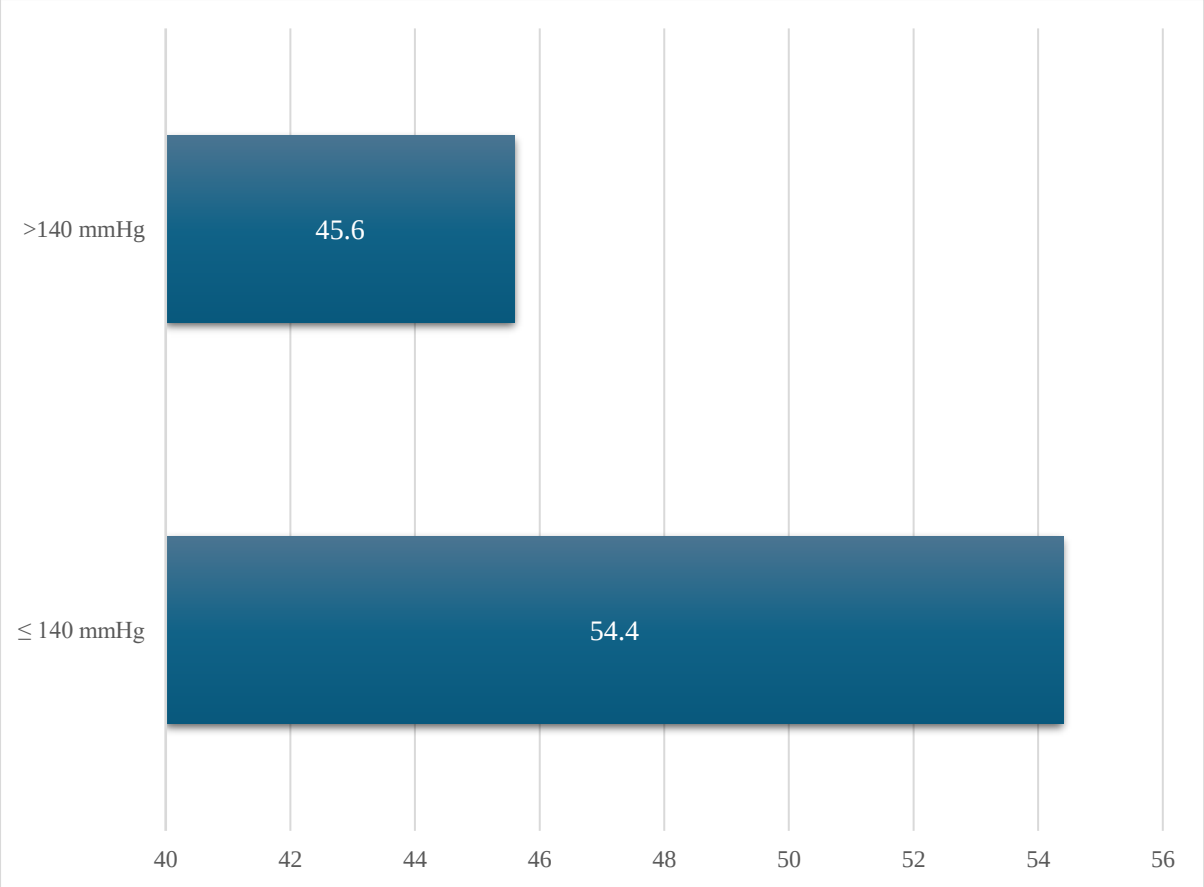


Graph 9: Bar graph showing the distribution of history of stroke among PEX patients

Only three patients (2.6%) had a previous history of stroke among all 114 participants. [Table 11] [Graph 9]

Table 12: Distribution of systolic blood pressure

SBP	Frequency(n)	Percentage (%)
≤ 140 mmHg	62	54.4
>140 mmHg	52	45.6
Total	114	100.0

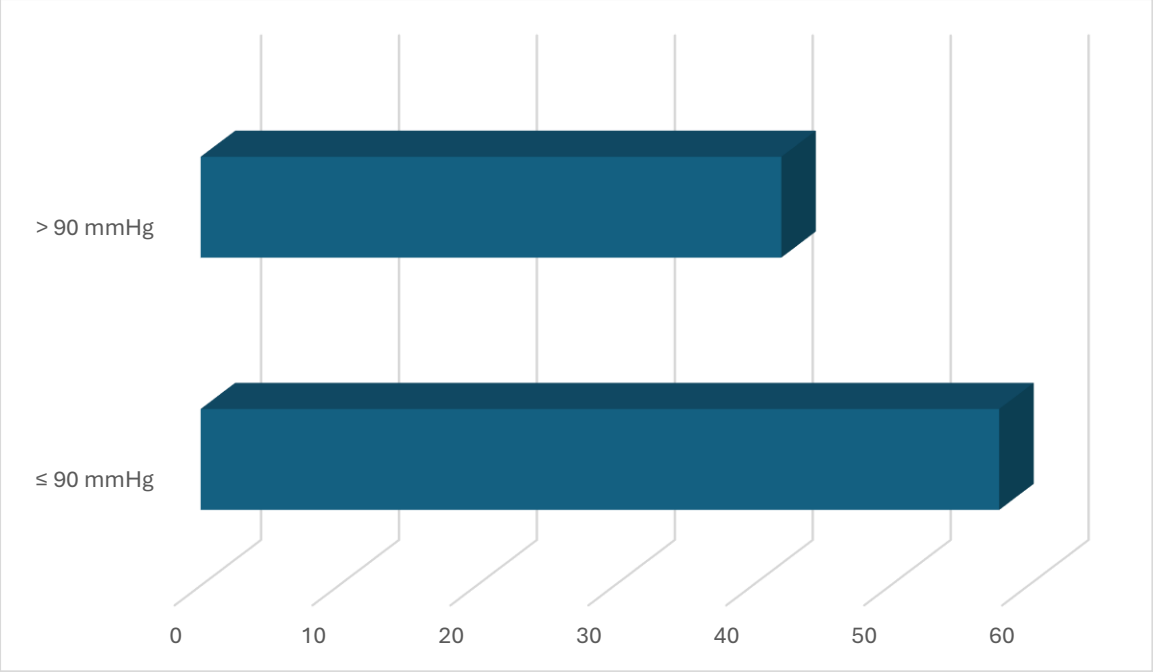


Graph 10: Bar graph showing the distribution of systolic blood pressure.

Fifty-two patients (45.6%) had a systolic blood pressure of more than 140 mmHg, while 62 (54.4%) had systolic blood pressure less than or equal to 140 mmHg. [Table 12] [Graph 10]

Table 13: Distribution of diastolic blood pressure

DBP	Frequency(n)	Percentage (%)
≤ 90 mmHg	66	57.9
> 90 mmHg	48	42.1
Total	114	100.0

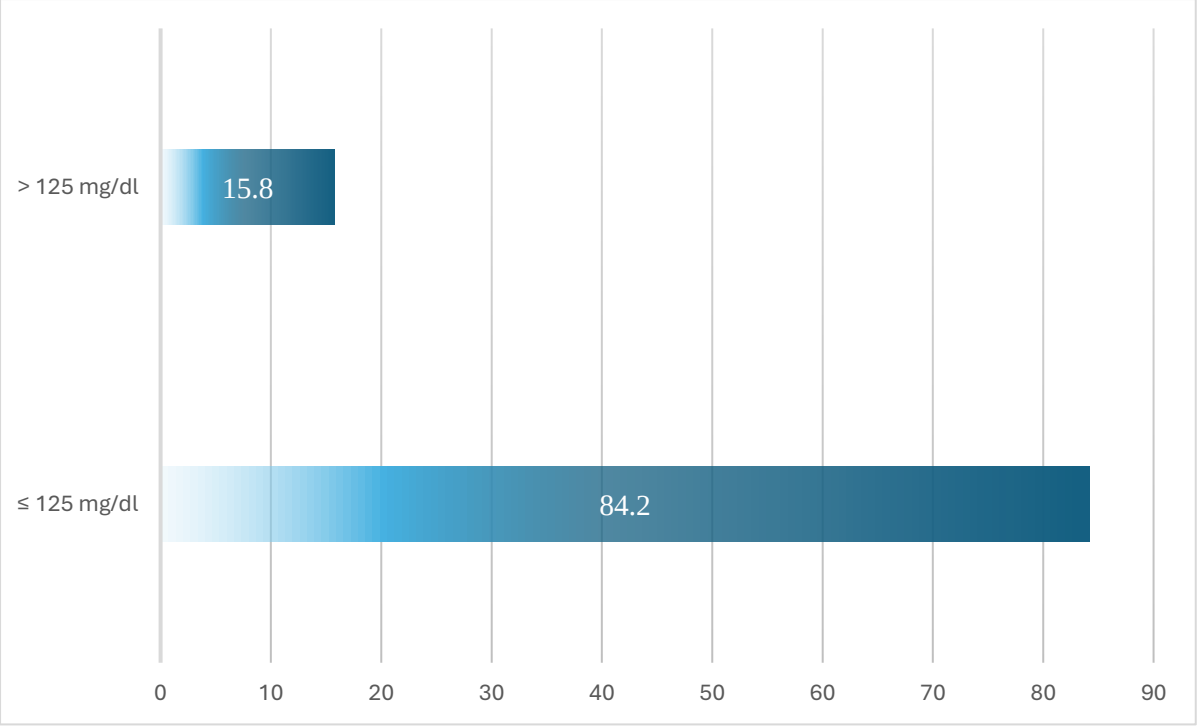


Graph 11: Bar graph showing the distribution of diastolic blood pressure.

Forty-eight patients (42.1%) had a diastolic blood pressure of more than 90 mmHg, while 66 (57.9%) had diastolic blood pressure lower than or equal to 90 mmHg. [Table 13] [Graph 11]

Table 14: Distribution of fasting blood sugar levels

FBS	Frequency(n)	Percentage (%)
≤ 125 mg/dl	96	84.2
> 125 mg/dl	18	15.8
Total	114	100.0

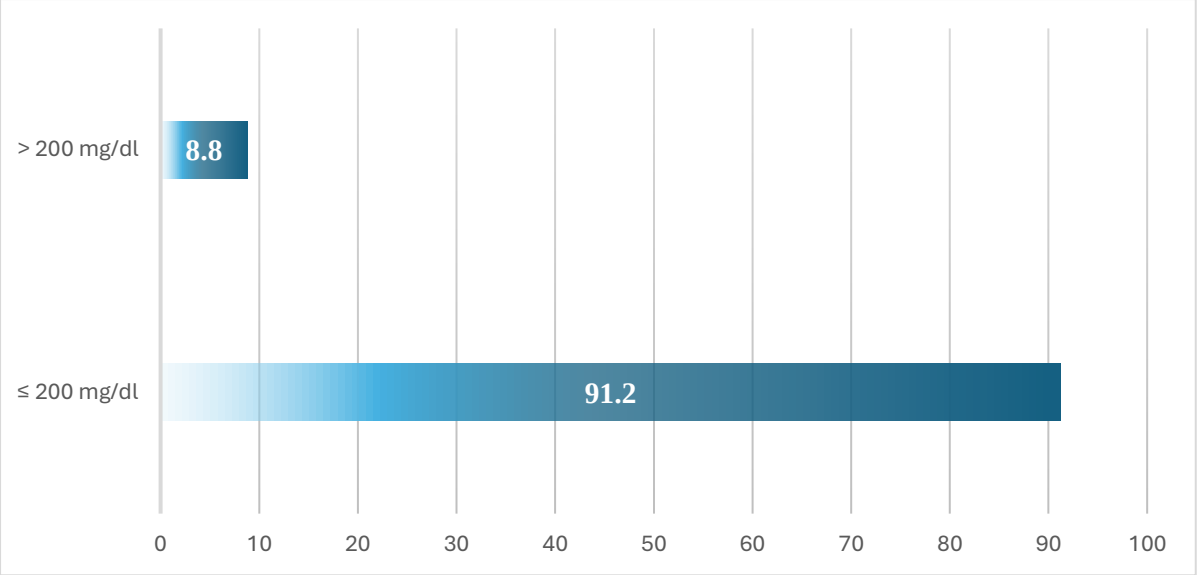


Graph 12: Bar graph showing the distribution of fasting blood sugar levels

Fasting blood sugar was more than 125 mg/dl in 18 participants (15.8%). However, 96 (84.2%) participants had fasting blood sugar less than or equal to 125 mg/dl. [Table 14] [Graph 12]

Table 15: Distribution of postprandial blood sugar levels

PPBS	Frequency(n)	Percentage (%)
≤ 200 mg/dl	104	91.2
> 200 mg/dl	10	8.8
Total	114	100.0

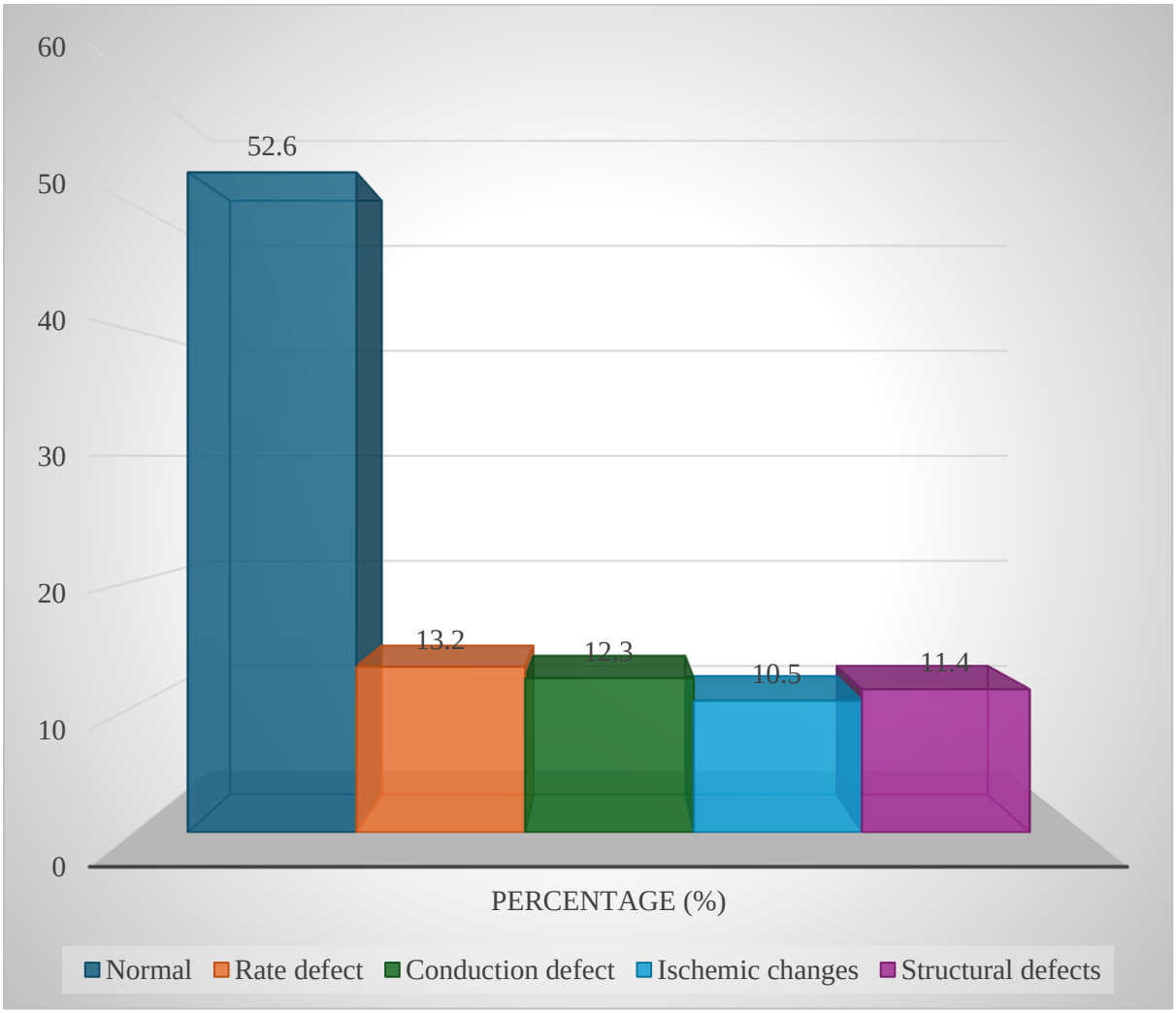


Graph 13: Bar graph showing the distribution of postprandial blood sugar levels

Postprandial blood sugar was more than 200 mg/dl in 10 patients (8.8%) and less than or equal to 200mg/dl in 104 (91.2%) participants. [Table 15] [Graph 13]

Table 16: Distribution of ECG changes

ECG changes	No. of patients	Percentage (%)
Normal	60	52.6
Rate defect	15	13.2
Conduction defect	14	12.3
Ischemic changes	12	10.5
Structural defects	13	11.4
Total	114	100.0

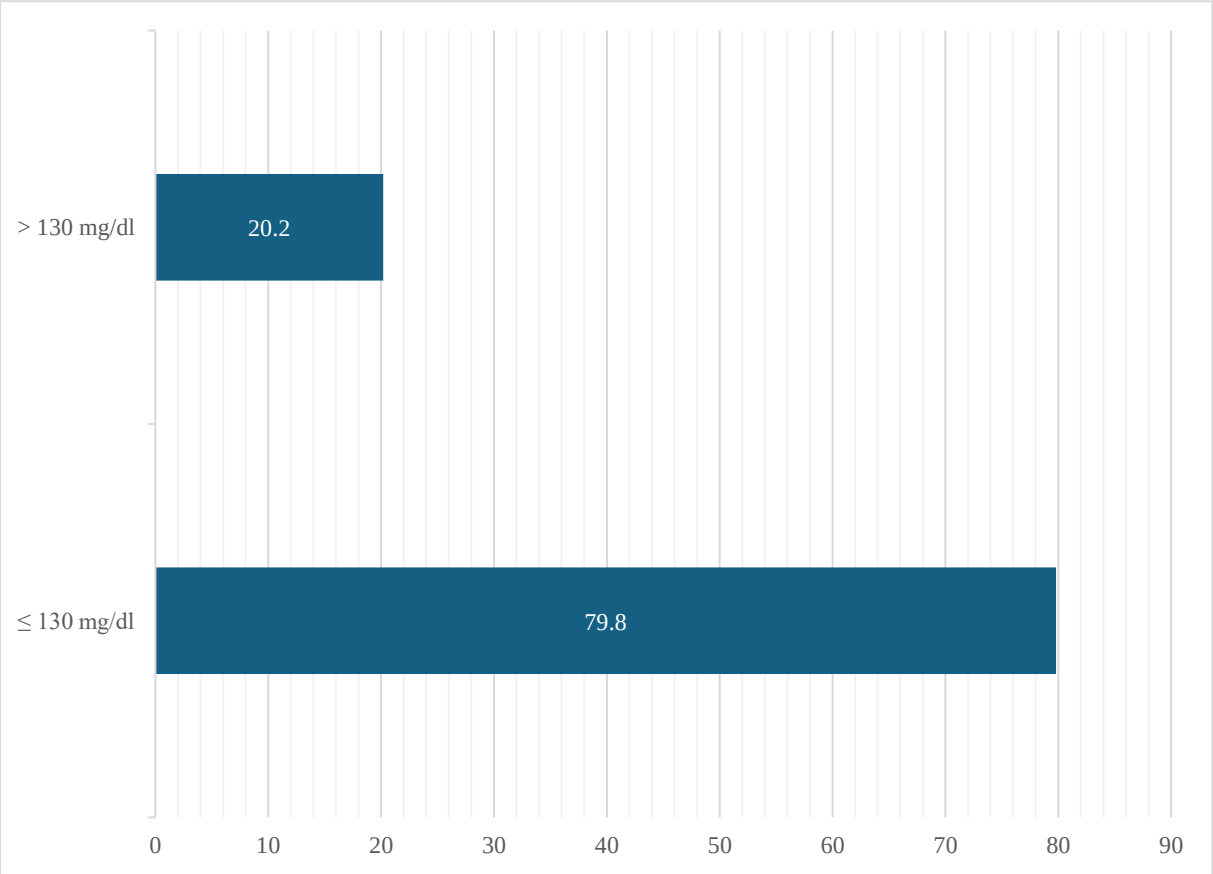


Graph 14: Bar graph showing the distribution of ECG changes

Among all 114 patients, 52.6% had normal ECG readings, indicating that more than half of the group exhibited no detectable abnormalities in their heart function. Rate defects were observed in 13.2% of the patients. Conduction defects, indicating delays or blocks in the electrical conduction system, were present in 12.3% of the patients. Ischemic changes were found in 10.5% of the patients. Structural defects were observed in 11.4% of the patients. [Table 16] [Graph 14]

Table 17: Distribution of serum LDL levels

LDL	Frequency(n)	Percentage (%)
≤ 130 mg/dl	91	79.8
> 130 mg/dl	23	20.2
Total	114	100.0

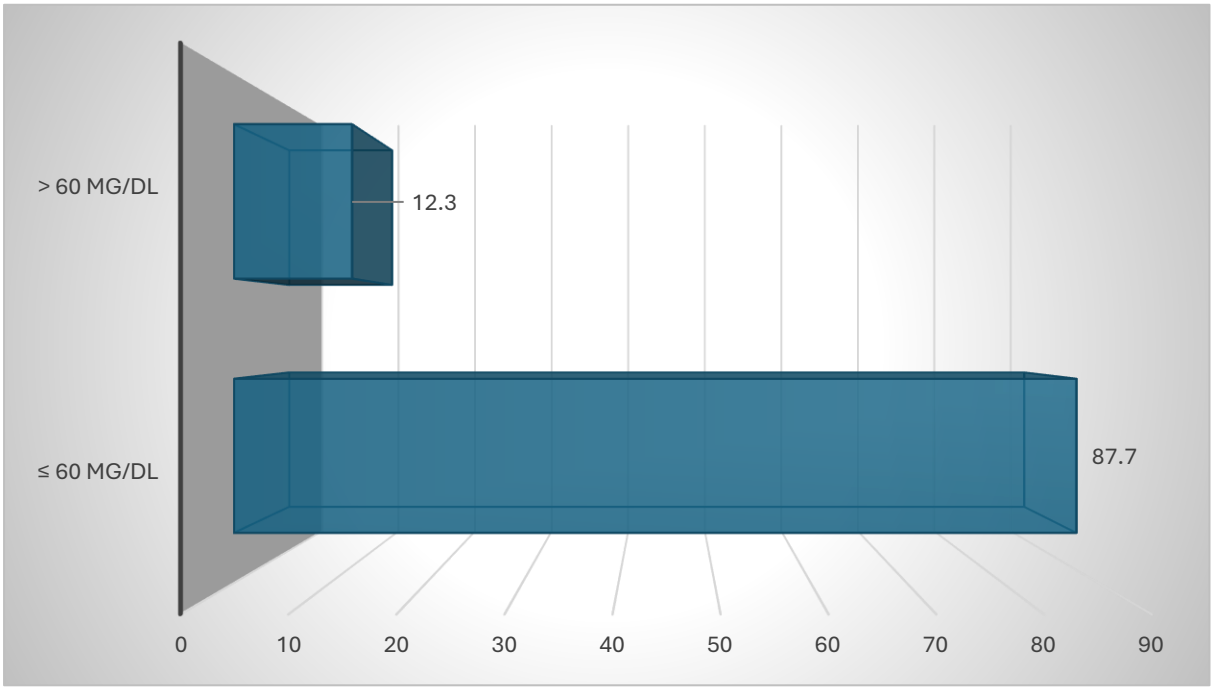


Graph 15: Horizontal bar graph showing LDL levels among participants.

Among all participants, 79.8% had LDL levels of 130 mg/dl or less. Conversely, 20.2% of the patients had LDL levels greater than 130 mg/dl, suggesting that a smaller portion of the group had elevated LDL levels, which may increase their risk of developing cardiovascular conditions. [Table 17] [Graph 15]

Table 18: Distribution of serum HDL levels

HDL	Frequency(n)	Percentage (%)
≤ 60 mg/dl	100	87.7
> 60 mg/dl	14	12.3
Total	114	100.0

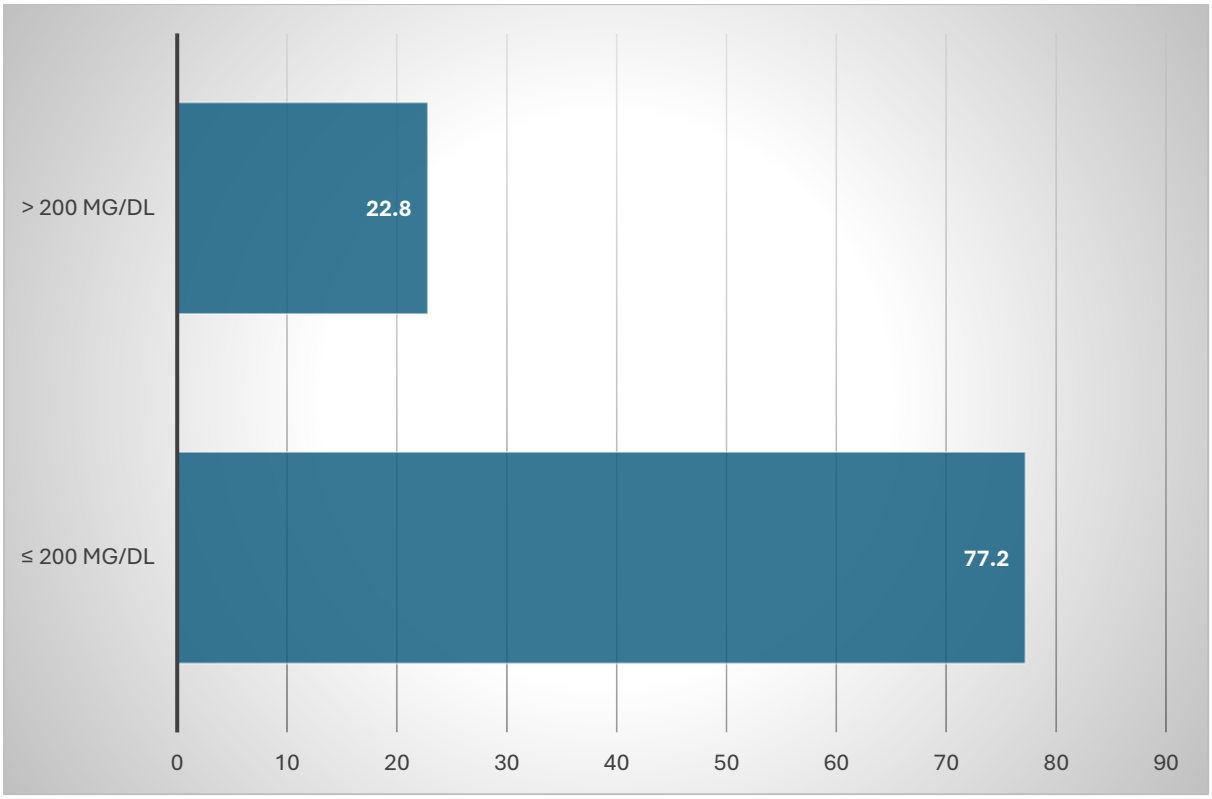


Graph 16: Horizontal bar graph showing HDL levels among participants.

HDL levels were less than or equal to 60 mg/dl in the majority of the participants (87.7%) and more than 60 mg/dl in 14 patients (12.3%). [Table 18] [Graph 16]

Table 19: Distribution of serum cholesterol levels

Total cholesterol	Frequency(n)	Percentage (%)
≤ 200 mg/dl	88	77.2
> 200 mg/dl	26	22.8
Total	114	100.0

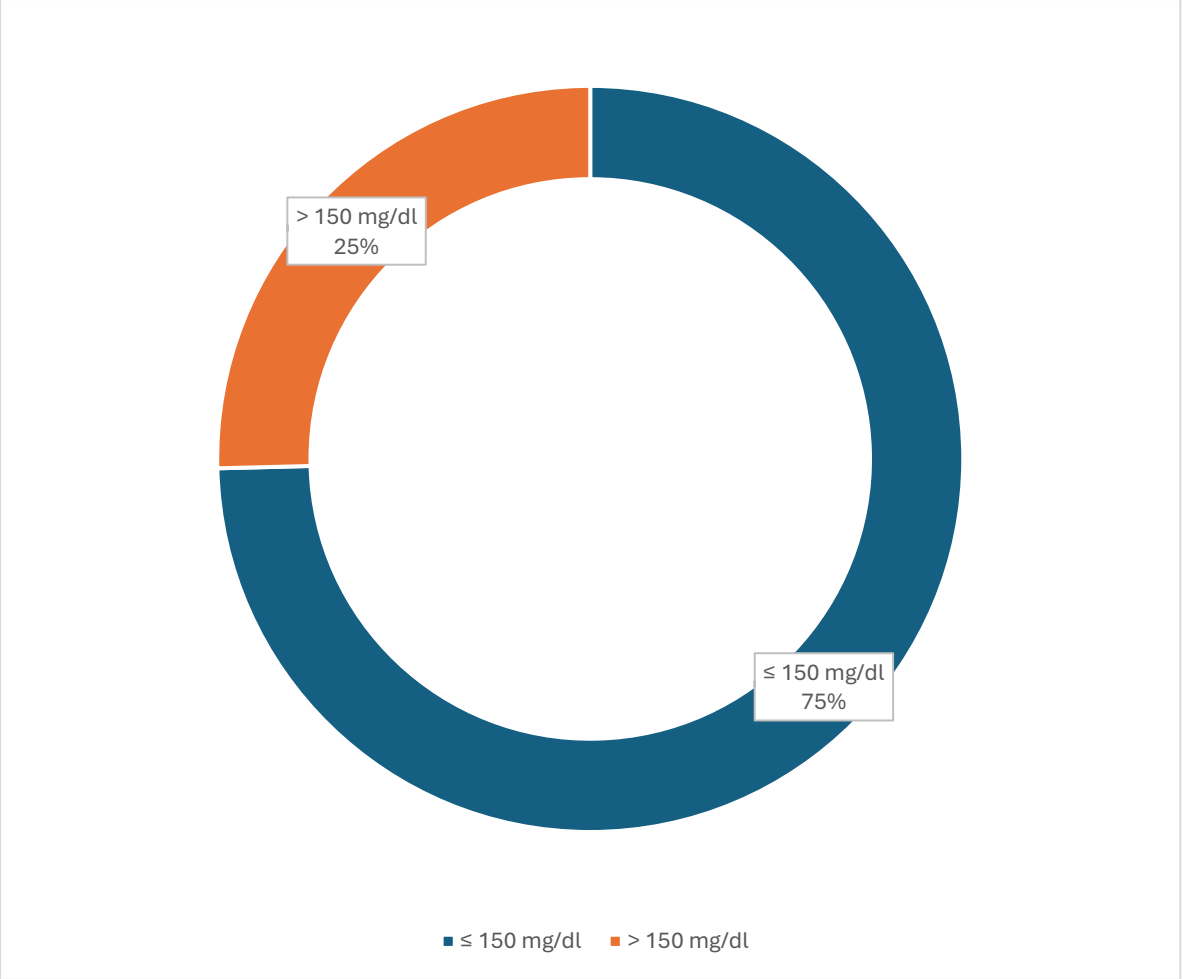


Graph 17: Horizontal bar graph showing cholesterol levels among participants.

Serum cholesterol levels were more than 200 mg/dl in 26 participants (22.8%) and less than or equal to 200mg/dl in 88 participants (77.2%). [Table 19] [Graph 17]

Table 20: Distribution of serum triglyceride levels

Total triglyceride	Frequency(n)	Percentage (%)
≤ 150 mg/dl	85	74.6
> 150 mg/dl	29	25.4
Total	114	100.0



Graph 18: Pie chart showing triglyceride levels among participants.

Among 114 participants, 85 (74.6%) had total triglyceride levels of 150 mg/dl or less. In contrast, 29 participants (25.4%) had total triglyceride levels exceeding 150 mg/dl. This indicates that most participants had triglyceride levels within the lower range, while a smaller portion had higher triglyceride levels. [Table 20] [Graph 18]

Table 21: Mean of different parameters among hypertensive and non-hypertensive participants.

Parameters	Hypertension	Frequency (n)	Mean	Standard deviation	P value
Fasting Blood Sugar	Yes	54	104.41	28.54	0.52
	No	60	103.25	34.73	
Post Prandial Blood Sugar	Yes	54	133.52	51.29	0.98
	No	60	130.10	45.69	
LDL	Yes	54	102.35	33.78	0.91
	No	60	103.58	35.39	
HDL	Yes	54	44.17	13.46	0.42
	No	60	46.48	17.18	
VLDL	Yes	54	30.11	26.99	0.45
	No	60	28.07	14.34	
Cholesterol	Yes	54	175.20	40.01	0.74
	No	60	170.50	46.35	
CRP	Yes	54	1.13	0.34	0.14
	No	60	1.05	0.22	
Triglyceride	Yes	54	131.83	76.43	0.66
	No	60	127.08	52.42	
Systolic blood pressure	Yes	54	146.00	10.70	*0.000***
	No	60	135.33	11.98	
Diastolic blood pressure	Yes	54	94.26	10.57	*0.000***
	No	60	86.87	10.35	

The study compared various systemic parameters between hypertensive and non-hypertensive participants. For fasting blood sugar, the hypertensive group had a mean value of 104.41 mg/dl

(SD = 28.540) compared to 103.25 mg/dl (SD = 34.728) in the non-hypertensive group, with a P value of 0.52, indicating no significant difference.

Post-prandial blood sugar levels were similar, with hypertensive participants having a mean of 133.52 mg/dl (SD = 51.293) and non-hypertensive participants having a mean of 130.10 mg/dl (SD = 45.693), resulting in a P value of 0.98. LDL levels were also comparable, with hypertensive participants having a mean of 102.35 mg/dl (SD = 33.778) and non-hypertensive participants 103.58 mg/dl (SD = 35.390) and a P value of 0.91. HDL levels showed a mean of 44.17 mg/dl (SD = 13.464) in hypertensive participants and 46.48 mg/dl (SD = 17.179) in non-hypertensive participants, with a P value of 0.42. VLDL levels were 30.11 mg/dl (SD = 26.991) in the hypertensive group and 28.07 mg/dl (SD = 14.337) in the non-hypertensive group, having a P value of 0.45.

Cholesterol levels were slightly higher in the hypertensive group (mean = 175.20 mg/dl, SD = 40.015) compared to the non-hypertensive group (mean = 170.50 mg/dl, SD = 46.349), with a P value of 0.74. CRP levels were 1.13 mg/L (SD = 0.339) in hypertensive participants and 1.05 mg/L (SD = 0.220) in non-hypertensive participants, with a P value of 0.14. Triglyceride levels were 131.83 mg/dl (SD = 76.432) in hypertensive participants and 127.08 mg/dl (SD = 52.417) in non-hypertensive participants, with a P value 0.66. Significant differences were observed in blood pressure measurements. Hypertensive participants had a mean systolic blood pressure of 146.00 mmHg (SD = 10.696) compared to 135.33 mmHg (SD = 11.975) in non-hypertensive participants, with a P value of 0.00, indicating a significant difference. Similarly, diastolic blood pressure was significantly higher in hypertensive participants, with a mean of 94.26 mmHg (SD = 10.569) compared to 86.87 mmHg (SD = 10.352) in non-hypertensive participants, and a P value of 0.00. These results highlight that hypertensive individuals, though on anti-hypertensive medications, had significantly higher

systolic and diastolic blood pressure compared to non-hypertensive individuals. At the same time, other vascular parameters showed no significant differences. [Table 21]

Table 22: Association of different systemic parameters with severity of PEX.

Systemic parameter	Severity of PEX			P-value
	Mild [n = 38]	**Moderate** [n = 44]	**Severe** [n = 32]	
SBP more than 140 mmHg	03 [7.9%]	20 [45.5%]	29 [90.6%]	*0.001****
DBP more than 90 mmHg	03 [7.9%]	19 [43.2%]	26 [81.3%]	*0.001****
Fasting blood sugar	03 [7.9%]	06 [13.6%]	09 [28.1%]	0.061
Postprandial blood sugar	02 [5.3%]	03 [6.8%]	05 [15.6%]	0.263
Serum Cholesterol of more than 200 mg/dl	09 [23.7%]	11 [25.0%]	06 [18.8%]	0.804
Serum LDL more than 130 mg/dl	10 [26.3%]	08 [18.2%]	05 [15.6%]	0.494
Serum Triglyceride more than 150 mg/dl	08 [21.1%]	10 [22.7%]	11 [34.4%]	0.386
C – Reactive protein of more than 10 mg/dl	02 [5.3%]	04 [9.2%]	04 [12.5%]	0.564
Electrocardiogram findings				
Normal	25 [65.8%]	23 [52.3%]	12 [37.5%]	0.418
Rate defects	05 [13.2%]	05 [11.4%]	05 [15.6%]	
Conduction defects	02 [5.3%]	07 [15.9%]	05 [15.6%]	
Ischemic defects	04 [10.5%]	04 [9.1%]	04 [12.5%]	
Structural defects	02 [5.3%]	05 [11.4%]	06 [18.8%]	

The study investigated the relationship between systemic parameters and pseudoexfoliation syndrome (PEX) severity, categorizing patients into mild, moderate, and severe PEX groups. The analysis revealed compelling associations between elevated blood pressure and PEX severity. Notably, systolic blood pressure (SBP) levels exceeding 140 mmHg were found in 7.9% of mild PEX cases, significantly rising to 45.5% in moderate cases and striking 90.6% in severe cases (P-value = 0.001). Similarly, diastolic blood pressure (DBP) levels above 90 mmHg showed a similar trend, with 7.9% in mild PEX, escalating to 43.2% in moderate cases and, notably, 81.3% in severe cases (P-value = 0.001).

Regarding blood sugar levels, although no statistically significant differences were observed in fasting blood sugar levels across PEX severity categories, there was a notable trend. Fasting blood sugar levels were reported in 7.9% of mild PEX cases, 13.6% of moderate cases, and 28.1% of severe cases (P-value = 0.061), indicating a possible association that warrants further investigation given the links between diabetes and vascular health.

In contrast, lipid profiles, including serum cholesterol, LDL (low-density lipoprotein), and triglyceride levels, did not differ significantly across PEX severity categories. For instance, serum cholesterol levels above 200 mg/dl were found in 23.7% of mild PEX cases, 25.0% of moderate cases, and 18.8% of severe cases (P-value = 0.804). Similarly, serum LDL levels above 130 mg/dl were reported in 26.3% of mild PEX cases, 18.2% of moderate cases, and 15.6% of severe cases (P-value = 0.494). Triglyceride levels above 150 mg/dl showed a similar pattern, with 21.1% in mild PEX, 22.7% in moderate cases, and 34.4% in severe cases (P-value = 0.386). These findings suggest that lipid profiles may not strongly correlate with the severity of PEX in this study cohort.

Furthermore, the inflammatory marker C-reactive protein (CRP) did not significantly vary across PEX severity categories. CRP levels above 10 mg/dl were observed

in 5.3% of mild PEX cases, 9.2% of moderate cases, and 12.5% of severe cases (P-value = 0.564), indicating that systemic inflammation measured by CRP may not be a significant factor in PEX severity. Finally, electrocardiogram (ECG) findings displayed diverse patterns across different PEX severity groups, including normal findings, rate defects, conduction defects, ischemic defects, and structural defects. However, the overall analysis did not reveal a significant association between ECG patterns and PEX severity (P-value = 0.418).

So, blood pressure levels, especially SBP and DBP, strongly correlate with PEX severity. Other systemic parameters such as blood sugar levels, lipid profiles, inflammatory markers (CRP), and ECG findings did not show consistent and significant associations in this study cohort. [Table 22]

Table 23: Complications in ocular pseudoexfoliation

Complications	Frequency[n]	Percentage [%]
Ocular Complications		
Non-dilating pupil and Iris atrophy	99	86.8
Zonular dialysis	15	13.2
Intraoperative complication		
Extension of capsulorhexis	78	68.4
Difficulty in nucleus prolapse	56	49.1
Posterior capsular rent	33	29.0
Aphakia	8	7.0
Nucleus drop	1	0.9

Patients with pseudoexfoliation syndrome (PEX) often experience a spectrum of ocular complications, as evidenced by [Table 22]. The most frequent ocular complication observed was a non-dilating pupil and iris atrophy, affecting 86.8% of the cases. Zonular dialysis, though less common, was still noted in 13.2% of cases. During intraoperative procedures, complications such as an extension of capsulorhexis, difficulty in nucleus prolapse, and posterior capsular rent were observed in 68.4%, 49.1%, and 29.0% of cases, respectively. Complications like aphakia (7.0%) and nucleus drop (0.9%) were less frequently encountered.

Discussion

The study aimed to investigate the relationship between systemic vascular disorders and pseudoexfoliation syndrome, particularly emphasizing the prevalence and ocular manifestations of PEX. We examined systolic and diastolic blood pressure, glycemic status, dyslipidemia, and cardiac anomalies as detected on electrocardiograms (ECG). Our findings indicated a significant elevation in diastolic and systolic blood pressure among patients with PEX, with the most severe cases showing the highest blood pressure readings. ECG abnormalities were more common in PEX patients, including rate, conduction, ischemic, and structural defects. Of 114 patients, 33.3% had mild PEX, 38.6% had moderate PEX, and 28.1% had severe PEX. [Figure 3]

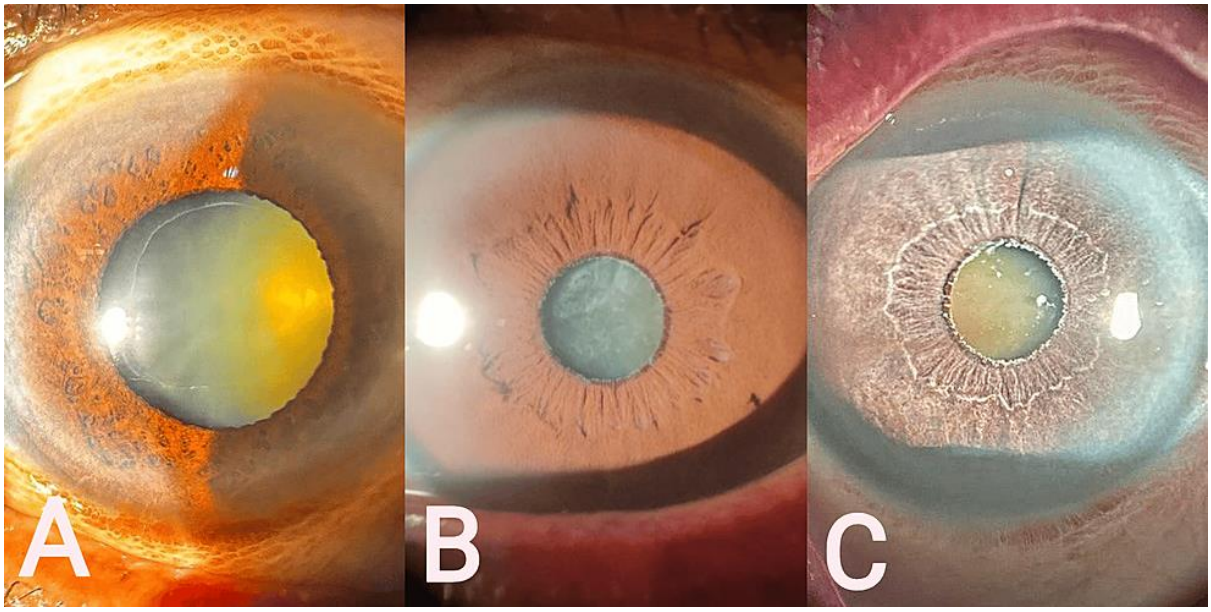


Figure 3: Grading of PEX as observed in our study. A: Mild; B: Moderate; C: Severe.

Hypertension was found in 47.4% of participants, diabetes in 18.4%, coronary artery disease in 7.9%, and cerebrovascular accidents in 2.6%. The diastolic and systolic mean blood pressures were 140.39 mmHg and 90.37 mmHg, respectively, with severe PEX patients

exhibiting significantly higher blood pressure levels. The mean fasting and postprandial blood sugar levels were 103.80 ± 31.81 mg/dl and 131.72 ± 48.24 mg/dl, respectively, showing no significant differences across PEX severity levels. ECG abnormalities were present in 47.37% of participants, underscoring the cardiovascular risks associated with PEX. While elevated blood pressure strongly correlated with PEX severity, other systemic parameters like blood glucose levels and ECG anomalies were prevalent but did not correlate significantly with PEX severity.

The average age of the participants in the Vardhan SA et al. study was reported to be 64.8 (± 6.8) years, suggesting a relatively younger cohort than other studies (19). In contrast, French D et al. reported a higher mean age of 77.1 (± 9.1) years, suggesting that their study population was predominantly older (55). Our study falls between these two, with a mean age of 68.95 (± 8.08) years, reflecting a more middle-aged to elderly population. According to Young A. et al., most patients were above 65 years old, which is consistent with our findings, where most participants were between 60 and 79 years old (31). The gender distribution of pseudoexfoliation varies among all studies. Vardhan SA et al. included 50.5% males and 49.5% females, showing an almost equal representation of both genders (19). This is similar to our study, where we included 56.1% males and 43.9% females, indicating a slightly higher proportion of male participants. However, Young A. et al. studied demographics in a Chinese cohort and noted a higher female preponderance, with 63% female participants (31). These comparisons show that age and gender are important when studying PEX, as different studies have varying ages and gender distributions, suggesting that PEX affects diverse populations.

The prevalence of PEX detected in our study is 3.52%. This contrasts with an Asian study by Young A. et al., who reported a prevalence of 0.4% in a Chinese cohort (31). Speckauskas M et al. found a higher prevalence of 9%, which is above our findings (56).

However, a study by Vardhan et al. conducted in southern India reported a varied prevalence ranging from 1.87% to 13.5%. (19).

In a Warjri G. et al. study, pseudoexfoliation material was most frequently observed at “the pupillary margin in 81.01% of cases”. This was followed by the involvement of “the rest of the iris in 19.15%, the lens in 5.72%, the anterior chamber angle in 1.12%, and the cornea in 0.99% of cases” (57). In contrast, our study found that the pupillary ruff and anterior lens capsule were the most commonly affected areas, seen in 94 cases (82.5%). Additionally, the endothelium was involved in 14 cases (12.3%), and the angle of the anterior chamber was affected in 6 cases (5.3%). These findings suggest that while there are similarities in the distribution of pseudoexfoliation material, the pupillary ruff and anterior lens capsule appear to be the primary sites of involvement in both studies, indicating their susceptibility to pseudoexfoliation syndrome.

In this study, we found that 47.4% of patients were hypertensive, a notably higher percentage compared to the study by Pooja H et al., who reported 14.92% hypertensive individuals (22). However, the percentage of people with diabetes was similar between our study and Pooja H et al., with our study reporting 25.37% diabetics and Pooja H et al. reporting 18.4% (22). Our study also noted that 7.9% of patients had a history of coronary artery disease, and 2.6% had a history of cerebrovascular accident. In comparison, Aristimuno N et al. reported that “3.7% of CAD patients and 4.6% of CVA patients” in their study (58). It sheds light on the variations in the prevalence of comorbidities such as hypertension, diabetes, CAD, and CVA across different studies, emphasizing the importance of considering such factors in understanding the broader clinical profile of patients with pseudoexfoliation syndrome.

Vardhan SA et al. reported a “mean systolic blood pressure (SBP) of 131.8 mmHg and diastolic blood pressure (DBP) of 78.1 mmHg” in their study (19). Conversely, Akarsu C

et al. reported a lower mean SBP of 120 mmHg and a slightly higher mean DBP of 80.5 mmHg in their research (59). Similarly, Aristimuno N et al. also documented mean SBP and DBP values, although the specific numbers are not mentioned in their text (58). Our study observed that 45.6% of patients had SBP levels exceeding 140 mmHg, indicating hypertension, while 42.1% had DBP levels surpassing 90 mmHg. These findings highlight the need for continuous monitoring and appropriate management of blood pressure in patients with pseudoexfoliation syndrome to mitigate associated cardiovascular risks, given the substantial proportion exhibiting elevated blood pressure.

The link between diabetes and pseudoexfoliation syndrome has long been a debate. A study by Vardhan SA et al. showed that PEX patients tend to have higher blood sugar levels, with random blood sugar levels averaging 125.2 (± 68.3) mmHg in PEX patients compared to 119.2 (± 51.6) mmHg in those without PEX (19). Our study investigated FBS and PPBS levels in PEX patients, revealing that 15.8% had FBS levels exceeding 125 mg/dl, and 8.8% had PPBS levels over 200 mg/dl. Akritidou F et al.'s research highlighted more severe degenerative changes in the lens cells of diabetic PEX patients than in those without diabetes (60). Additionally, Yu et al.'s meta-analysis found no overall association between diabetes mellitus and pseudoexfoliation syndrome, but they noted an inverse relationship in older populations and case-control studies (61). These studies collectively highlight the significant impact of diabetes on pseudoexfoliation syndrome and emphasize the importance of managing blood sugar levels in individuals with PEX to mitigate associated risks.

Mitchell P et al. and Citirik M et al. reported "a positive correlation between pseudoexfoliation (PEX) and coronary artery disease." However, they did not specify the types of coronary defects involved (62,63). In contrast, Vardhan SA et al. identified a "higher incidence of left ventricular hypertrophy in PEX patients than controls, with a statistically significant p-value of 0.02" (19). Our study further supports these findings, with 54 patients

(47.37%) exhibiting abnormal ECG results. Specifically, 13.2% had rate defects, 12.3% had conduction defects, 10.5% had ischemic changes, and 11.4% had structural defects. It highlights the diverse and significant cardiovascular anomalies associated with PEX, supporting these patients' need for comprehensive cardiovascular monitoring.

Several studies have explored the relationship between pseudoexfoliation syndrome and serum lipid levels, highlighting significant associations that could impact patient management. Kurtul et al. divided their study participants into three groups—patients with PEX, PEX glaucoma, and controls—and found that "mean LDL values were significantly higher in PEX groups" (138 ± 33 mg/dl and 150 ± 37 mg/dl) compared to controls (127 ± 36 mg/dl) with a p-value of 0.04. They also noted a higher frequency of diabetes and hypertension among PEX patients, suggesting a link between elevated LDL levels and PEX (20). Mirza et al. investigated traditional and non-traditional lipid profiles in PEX patients, finding significantly "higher median values of TC, TG, LDL-c, HDL-c, and non-HDL-c in the PEX group." However, the study concluded that non-traditional lipid ratios were more effective in identifying vascular disease risk (64). Khataminia et al. focused on cataract patients with and without PEX, revealing "significantly higher TG levels in the PEX group but no significant differences in other lipid levels" (65).

Lesiewska et al. found "no significant differences in lipid concentrations or CRP levels between PEX patients and controls," challenging the link between PEX and vascular diseases (66). Abay and Katipoğlu highlighted the TyG index as a marker for vascular risk, showing a significantly higher TyG index in PEX patients (67). Among all patients in our study, 79.8% had LDL levels of 130 mg/dl or less, while 20.2% had levels greater than 130 mg/dl, indicating a cardiovascular risk. Furthermore, 87.7% had HDL levels of 60 mg/dl or less, and 12.3% had levels greater than 60 mg/dl. Serum cholesterol levels were over 200 mg/dl in 22.8%

of patients, and 25.4% had triglyceride levels exceeding 150 mg/dl, suggesting a notable proportion of patients with elevated lipid levels that could pose cardiovascular risks.

Our study observed that the most common ocular complication in patients with pseudo-exfoliation syndrome undergoing cataract surgery was a non-dilating pupil and iris atrophy, affecting 86.8% of cases. This aligns with the findings of Egemen et al., who also noted a higher incidence of poor intraoperative pupil dilation in PEX patients compared to controls (68). Additionally, we found that although less common, zonular dialysis was still present in 13.2% of cases. This is consistent with the emphasis on zonular weakness as a significant risk factor in PEX patients highlighted in both our study and the study conducted by Thevi T et al.(69). In our study, during intraoperative procedures, complications such as an extension of capsulorhexis, difficulty in nucleus prolapse, and posterior capsular rent were observed in 68.4%, 49.1%, and 29.0% of cases, respectively, indicating a higher rate of intraoperative challenges in PEX patients.

Aoki et al. investigated “corneal endothelial cell density (ECD) in patients with pseudoexfoliation syndrome.” They analyzed data from “51 eyes of 41 phakic patients with PEX (PEX group)” and compared it with “201 eyes of 117 patients with age-related cataracts (control group)”. The “mean ECD in the PEX group was significantly lower at 2,548 ± 409 cells/mm² compared to the control group’s 2,757 ± 282 cells/mm²” ($P = 0.02$), indicating a notable reduction in corneal endothelial cells associated with PEX. Moreover, they categorized PEX severity into mild, moderate, and severe based on clinical factors. They found that the “severity of PEX was significantly associated with lower ECD,” highlighting the progressive impact of PEX on corneal health. Comparing this with our study, where we also categorized patients into mild, moderate, and severe PEX groups, we observed similar trends regarding the impact of PEX severity on ocular complications. Specifically, our study revealed strong correlations between elevated blood pressure levels and the severity of PEX-related ocular

complications, with systolic blood pressure (SBP) and diastolic blood pressure (DBP) showing significant increases as PEX severity progressed. For instance, SBP levels exceeding 140 mmHg were found in 7.9% of mild PEX cases, escalating to 45.5% in moderate cases and a remarkable 90.6% in severe cases (P-value = 0.001). The corresponding trends were observed for DBP, emphasizing the importance of systemic parameters in understanding and managing PEX-related ocular conditions.

These findings highlight the clinical relevance of assessing PEX severity and its associations with ocular complications. In our study, we also did not find significantly elevated CRP among PEX cases, and CRP was not associated with the severity of PEX. Our findings aligned with the studies by Yuksel N et al., Lesiewska et al., Sorkhabi et al., and Kymionis et al.(18,70–72).

The limitations of our study were a comparably smaller sample size and not comparing our data with non-PEX counterparts. More studies are sought to address these gaps in the future.

Conclusion

This study highlights significantly deranged parameters of systemic vascular diseases in PEX patients. Patients with PEX exhibited elevated systolic and diastolic blood pressure, which increased with the severity of PEX and more frequent cardiac anomalies as detected by ECG. These findings indicate the importance of comprehensive systemic evaluation in patients with PEX, particularly in older populations. The ocular complications associated with PEX, such as non-dilating pupils, iris atrophy, and intraoperative challenges during cataract surgery, also emphasize the need for careful preoperative assessment and planning. The study calls for further research to explore the systemic implications of PEX and to develop strategies for early detection and management of associated conditions, particularly in regions with limited data, such as southern India. Early identification of PEX through slit-lamp examinations can be critical in recognizing individuals at increased risk for systemic diseases, potentially improving public health outcomes and clinical care for affected individuals.

Appendix I

Consent form

STUDY SUBJECT CONSENT FORM

I confirm that Dr VAISHNAVI R. PATIL has explained the purpose of the research, the study procedure, the benefits, and the possible discomfort that I may experience in the language best understood by me. Therefore, I agree to participate as a subject in this research project and willfully consent.

_____ _____

(Participant) (Date)

_____ _____

(Witness to above signature) (Date)

ಅಧ್ಯಯನವಿಷಯಕಾನ್ಸೆಂಟ್ಫಾರ್ಮ್

ಡಾ. ವೈಷ್ಣವಿ ರಾಮೇಶ್ವರ ಪಾಟೀಲ್, ನನಗೆ ಸಂಶೋಧನೆಯ ಉದ್ದೇಶ, ಅಧ್ಯಯನದ ವಿಧಾನ ಮತ್ತು ಸಂಭವನೀಯ ಅಸ್ವಸ್ಥತೆಗಳು ಮತ್ತು ನನ್ನ ಸ್ವಂತಭಾಷೆಯಲ್ಲಿ ನಾನು ಅನುಭವಿಸಬಹುದಾದ ಪ್ರಯೋಜನಗಳನ್ನು ವಿವರಿಸಿದ್ದೇನೆ ಎಂದು ನಾನು ಖಚಿತ ಪಡಿಸುತ್ತೇನೆ. ಮೇಲಿನ ಎಲ್ಲಾ ವಿಷಯಗಳನ್ನು ನನ್ನ ಸ್ವಂತ ಭಾಷೆಯಲ್ಲಿ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ ಮತ್ತು ನಾನು ಅದನ್ನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ. ಆದ್ದರಿಂದ, ಈ ಸಂಶೋಧನಾಯೋಜನೆಯಲ್ಲಿ ವಿಷಯವಾಗಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪಿಗೆ ನೀಡಲು ನಾನು ಒಪ್ಪುತ್ತೇನ

(ಭಾಗವಹಿಸುವವರು) (ದಿನಾಂಕ)

Appendix II

Institutional Ethical Clearance

BLDE
(DEEMED TO BE UNIVERSITY)
Declared as Deemed to be University u/s 3 of UGC Act, 1956
Accredited with 'A' Grade by NAAC (Cycle-2)
The Constituent College
SHRI B. M. PATIL MEDICAL COLLEGE, HOSPITAL & RESEARCH CENTRE, VIJAYAPURA

BLDE (DU)/IEC/ 687/2022-23 30/8/2022

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this University met on **Friday, 26th August, 2022 at 3.30 p.m. in the Department of Pharmacology** scrutinizes the Synopsis of Post Graduate Student of BLDE (DU)'s Shri B.M.Patil Medical College Hospital & Research Centre from ethical clearance point of view. After scrutiny, the following original/ corrected and revised version synopsis of the thesis/ research projects has been accorded ethical clearance.

TITLE: "A PROSPECTIVE CROSS-SECTIONAL STUDY OF CORRELATION OF OCULAR PSEUDOEXFOLIATION WITH SYSTEMIC VASCULAR DISEASES".

NAME OF THE STUDENT/PRINCIPAL INVESTIGATOR: Dr. Patil Vaishnavi R

NAME OF THE GUIDE: Dr. Vallabha K,Professor & HoD, Dept. of Ophthalmology

Dr. Santoshkumar Jeevangi
Chairperson
IEC, BLDE (DU),
VIJAYAPURA

Chairman,
Institutional Ethical Committee,
BLDE (Deemed to be University)
Vijayapura

Dr.Akram A. Naikwadi
Member Secretary
IEC, BLDE (DU),
VIJAYAPURA

MEMBER SECRETARY
Institutional Ethics Committee
BLDE (Deemed to be University)
Vijayapura-586103. Karnataka

Following documents were placed before Ethical Committee for Scrutinization

- Copy of Synopsis/Research Projects
- Copy of inform consent form
- Any other relevant document

Smt. Bangaramma Sajjan Campus, B. M. Patil Road (Sholapur Road), Vijayapura - 586103, Karnataka, India.
BLDE (DU): Phone: +918352-262770, Fax: +918352-263303, Website: www.bldedu.ac.in, E-mail:office@bldedu.ac.in
College: Phone: +918352-262770, Fax: +918352-263019, E-mail: bmpmc.principal@bldedu.ac.in

Appendix III [Case proforma]

B.L.D.E (Deemed to be University)
Shri B.M.Patil Medical College Hospital And Research Centre,
Vijayapura-586103
Department Of Ophthalmology

CASE PROFORMA

Case No: ☐☐☐

Name : ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

Age: ☐☐ years Sex: ☐ (1-Male 2-Female) IP no: ☐☐☐☐☐☐☐

Address: ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐
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Contact no: ☐☐☐☐☐☐☐☐☐☐ / ☐☐☐☐☐☐☐☐☐☐

Date of admission: ☐☐■☐☐■☐☐☐ Date of Discharge ☐☐■☐☐■☐☐☐

Is the patient eligible for study? (1-Yes, 2-No): ☐

Has informed consent been given? (1-Yes, 2-No): ☐

Chief Complaints:

1. Diminution of vision: Right Eye ☐ Duration: ☐☐ days/months/years
   Left Eye ☐ Duration: ☐☐ days/months/years
2. Others (if any):
   ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

History of Present Illness:

1. Diminution of vision: Insidious (1) or Sudden (2): ☐
   Progressive (1) or Non-progressive (2): ☐
   Painless (1) or Painful (2): ☐
   For distance (1) or For near (2): ☐
2. Diplopia / Polyopia: Present (1) or Absent (2): ☐
3. Coloured halos: Present (1) or Absent (2): ☐
4. Black spots / non seeing area before eye
   Present (1) or Absent (2): ☐
5. Redness: Present (1) or Absent (2): ☐
6. Watering: Present (1) or Absent (2): ☐
7. Discharge: Present (1) or Absent (2): ☐
8. Pain in eyes: Present (1) or Absent (2): ☐
9. Headache: Present (1) or Absent (2): ☐
10. H/O present trauma: Present (1) or Absent (2): ☐
11. H/O wearing glasses: Present (1) or Absent (2): ☐
    Near (1) or Far (2) or Both (3): ☐
    Duration: ☐

Past history:

1. H/O past trauma to eye: Present (1) or Absent (2): ☐
2. Ocular surgery: Present (1) or Absent (2): ☐
   Type of surgery:……
   When performed ? : ……..
3. Diabetes: Present (1) or Absent (2): ☐
   Duration:……..
   Medication:……..
4. Hypertension: Present (1) or Absent (2): ☐
   Duration:……..

Medication:……..

5. CAD: Present (1) or Absent (2): ☐

Duration:……..

Medication:……..

6. Any other medical disorder:……

Personal History:

1. Smoking: Present (1) or Absent (2): ☐

Duration:……..

2. Alcohol intake: Present (1) or Absent (2): ☐

Duration:……..

3. Diet: Vegetarian(1) or Non Vegetarian (2) or Mixed (3): ☐

General Physical Examination:

1. Built: ☐

(Well built – 1, Moderately built – 2, Poorly built – 3, Emaciated – 4)

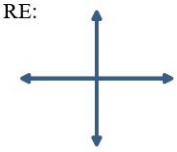
2. Pallor: Present (1) or Absent (2): ☐
3. Icterus: Present (1) or Absent (2): ☐
4. Clubbing: Present (1) or Absent (2): ☐
5. Koilonychia: Present (1) or Absent (2): ☐
6. Cyanosis: Present (1) or Absent (2): ☐
7. Lymphadenopathy: Present (1) or Absent (2): ☐
8. Edema: Present (1) or Absent (2): ☐
9. Pulse: ☐ /minute
10. Temperature: ☐ degree Fahrenheit
11. Blood pressure: ……../……mmHg
12. Respiratory rate: ☐ cycles per minute

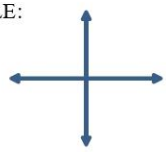
Systemic Examination:

1. CVS: ☐ Normal – 1, Abnormal – 2
   If 2, specify:……
2. CNS: ☐ Normal – 1, Abnormal – 2
   If 2, specify:……
3. Respiratory System ☐ Normal – 1, Abnormal – 2
   If 2, specify:……
4. Per abdomen: ☐ Normal – 1, Abnormal – 2
   If 2, specify:……

Ocular Examination:

- Head posture: 1 – Erect, 2 – Tilted ☐
- Visual axis: 1 – Parallel, 2 – Deviated ☐
- Facial Symmetry: 1 – Symmetrical 2 – Asymmetrical ☐
- Ocular motility: 1 – Normal (N) , 2 – Restricted (R) ☐

RE: 

LE: 

BINOCULAR: 

- Visual Acuity:

	RE	LE
DISTANT		
PINHOLE		
NEAR		
AIDED		

- Refraction:

Prescription	Spherical	Cylindrical	Axis	BCVA
RE				
LE				

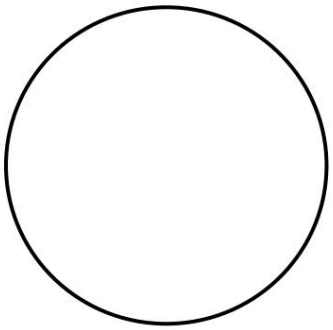
• **Adnexa:** 1- Normal 2- Abnormal	☐	☐
• **Sclera:** 1- Normal 2- Congested	☐	☐
• **Conjunctiva** 1- Normal 2- Conjunctival Congestion 3- Ciliary congestion 4- Chemosis	☐	☐

• **Cornea** 1- Normal 2- Opacity 3- Vascularization	☐	☐
• **Anterior Chamber** 1- Normal depth 2- Shallow 3- Deep	☐	☐
• **Iris** 1- Normal colour and pattern 2- Abnormal	☐	☐
• **Pupil** **Shape:** 1-Round and regular; 2- Irregular **Reaction:** Direct: 1-Present; 2-Absent Indirect: 1-Present; 2-Absent Near reflex: 1-Present; 2-Absent **Pseudo exfoliation granules in margin** 1- Present 2- Absent	**Size**:……mm ☐ ☐ ☐	**Size**:……mm ☐ ☐ ☐

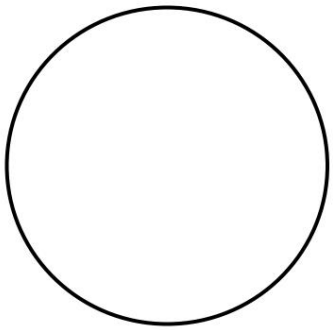
Grading of PEX: 1- Mild, 2- Moderate, 3- Severe	☐	☐
• **Lens** **Clarity:** 1-Clear; 2-Opaque 1- Cataract; 2- PCIOL If cataract present: 1- Immature 2- Mature 3- Hyper mature A) **Cortical cataract** (1-Present;2-Absent) B) **Nuclear sclerosis** (1-Present; 2-Absent) If present: GRADE: 1- Grade 1 2- Grade 2 3- Grade 3 4- Grade 4 C) **Posterior Sub capsular cataract** (1-Present 2-absent)	☐ ☐ ☐ ☐ ☐ ☐ ☐	☐ ☐ ☐ ☐ ☐ ☐ ☐
• **Lacrimal duct patency** (1-Patent, 2-Regurgitation, 2A-Clear fluid; 2B-Mucopurulent; 2C- Blocked)	☐	☐

FUNDUS EXAMINATION:

Fundus	Right eye	Left eye
Glow		
Media		
Disc		
CD ratio		
Blood vessels		
Background		
Macula		



RIGHT EYE



LEFT EYE

DIAGNOSIS:

PERIOPERATIVE COMPLICATIONS ('✓' if present)

- Preoperative:
  1. Non-dilating pupil; Iris atrophy:
  2. Zonular dialysis:
- Intraoperative:
  1. Extension of capsulorhexis:
  2. Difficulty in nucleus prolapse:
  3. Posterior capsular rent:
  4. Aphakia:
  5. Nucleus drop:

INVESTIGATIONS:

Investigations	Obtained value	Reference value
Fasting blood sugar(mg/dl)		< 125 mg/dl
Postprandial blood sugar(mg/dl)		<200 mg/dl
LDL(mg/dl)		< 130 mg/dl
HDL (mg/dl)		> 60 mg/dl
Cholesterol(mg/dl)		< 200 mg/dl
Triglyceride(mg/dl)		<150 mg/dl
CRP(mg/L)		< 10 mg/dl
ECG FINDINGS		

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Appendix IV

Colour plates

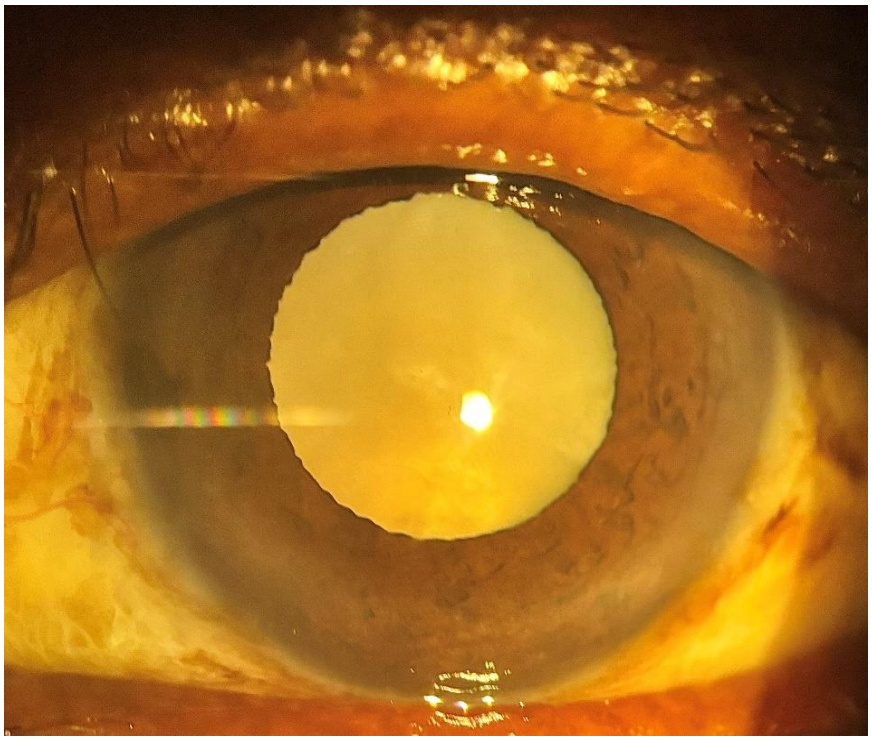

Figure 4: Mild PEX with mature cataract and 6 mm maximum pupillary dilatation.

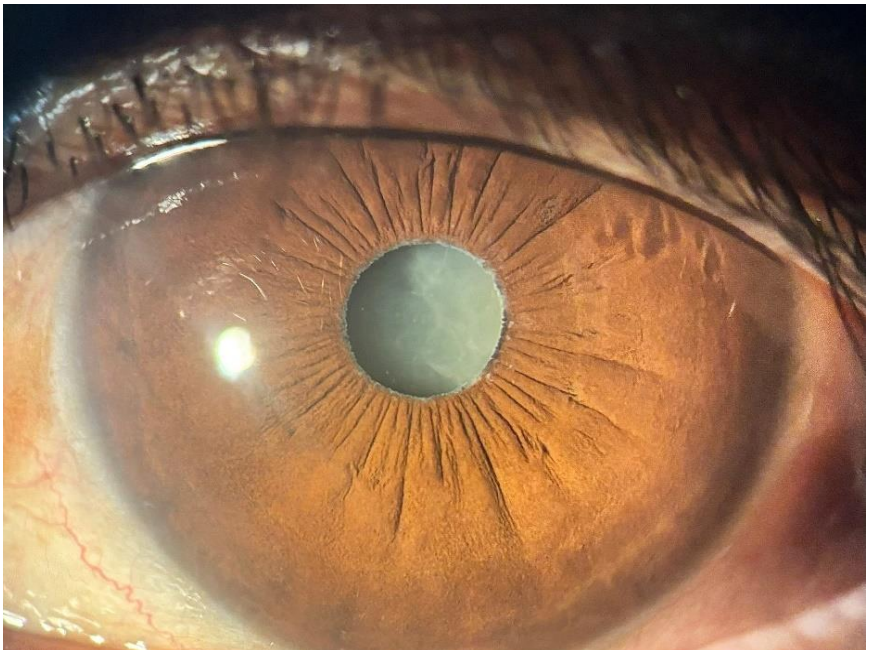

Figure 5: Severe PEX with mature cataract

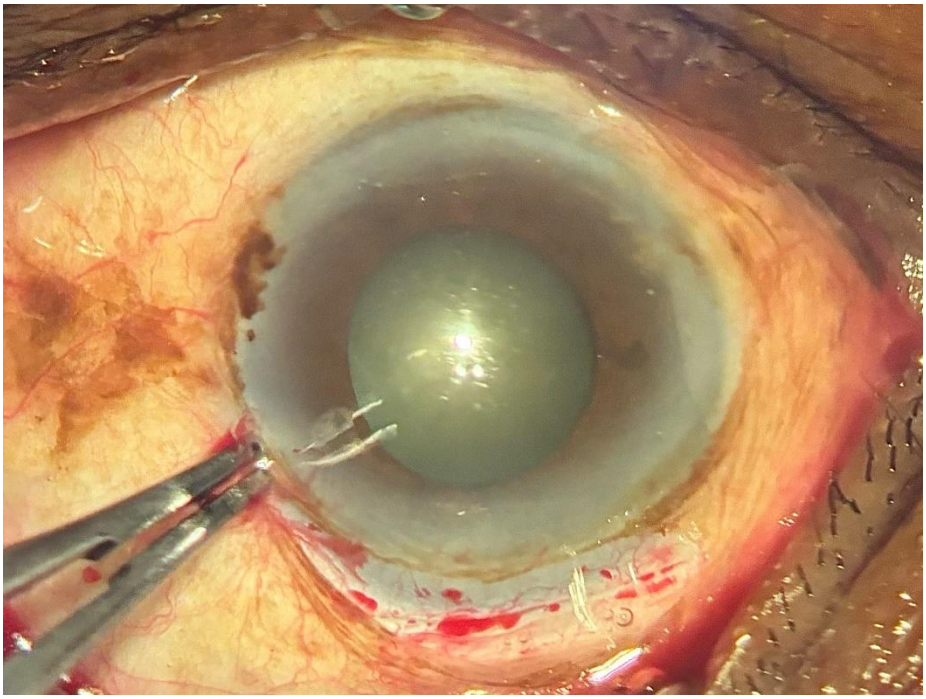

Figure 6: Intraoperative picture of mild PEX with immature cataract and 5 mm maximum pupillary dilatation.

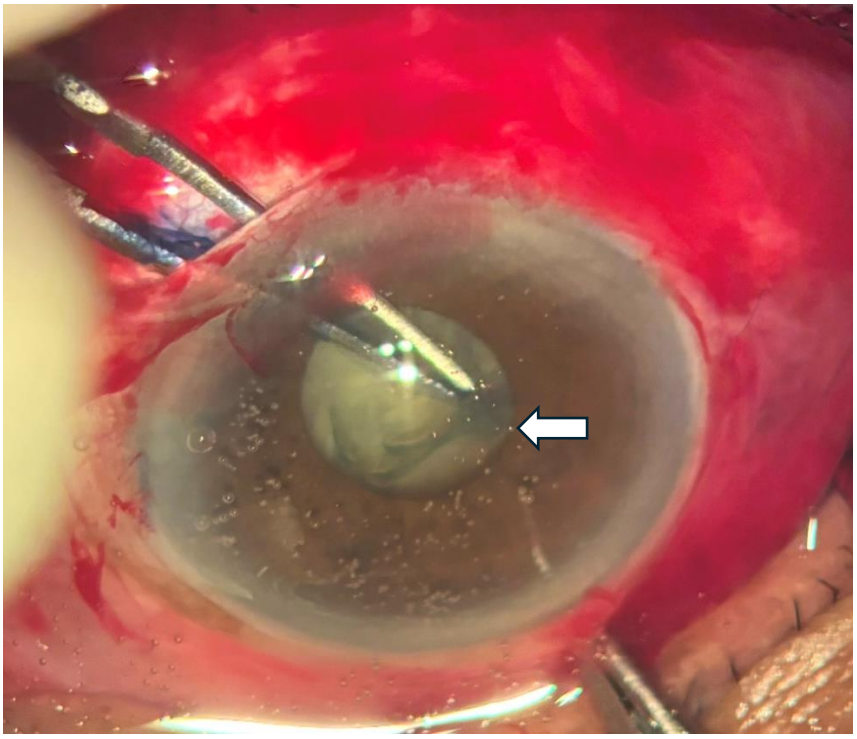

Figure 7: Extension of capsulorhexis in case of mild PEX with immature cataract and 4 mm maximum dilatation of the pupil (White arrow).

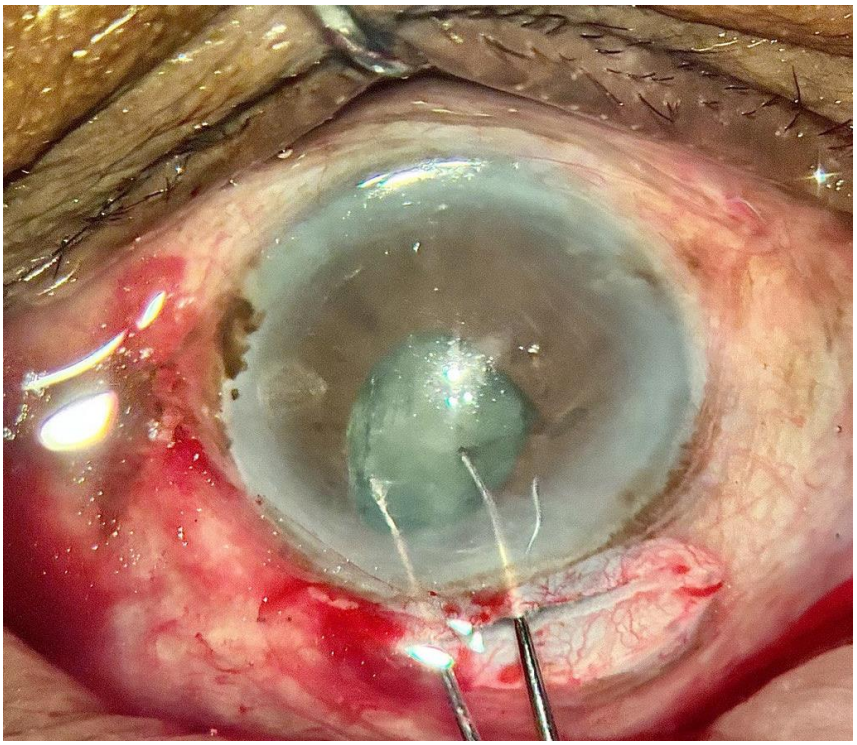

Figure 8: Difficulty prolapsing the nucleus in case of mild PEX with iris atrophic patches and 4 mm dilated pupil.

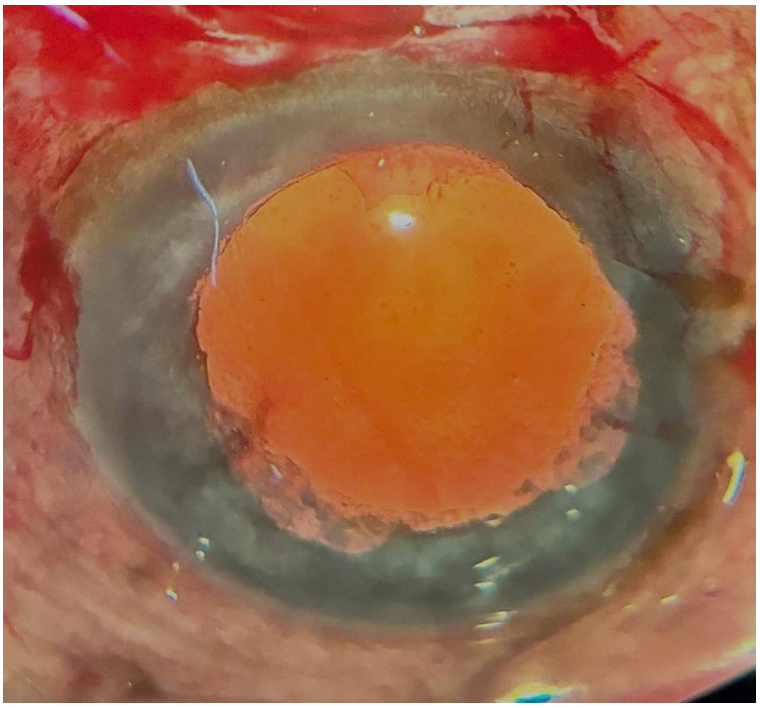

Figure 9: Intraoperative picture showing 7 mm dilated pupil, atrophic patches and transillumination defects in the iris in moderate PEX.

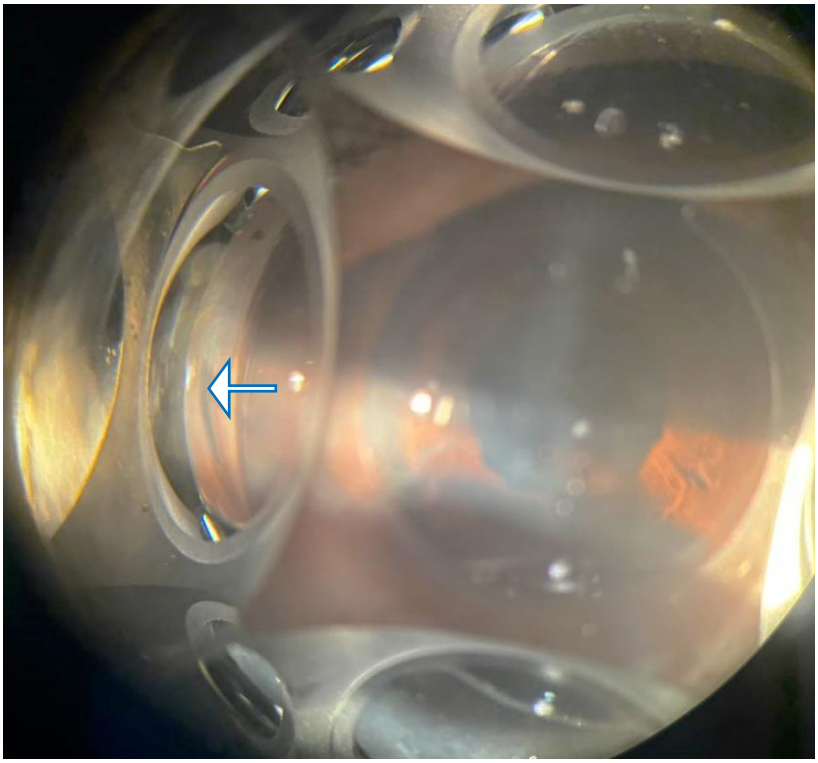

Figure 10: Sampaolesi line on gonioscopy in moderate PEX with immature cataract (White arrow).

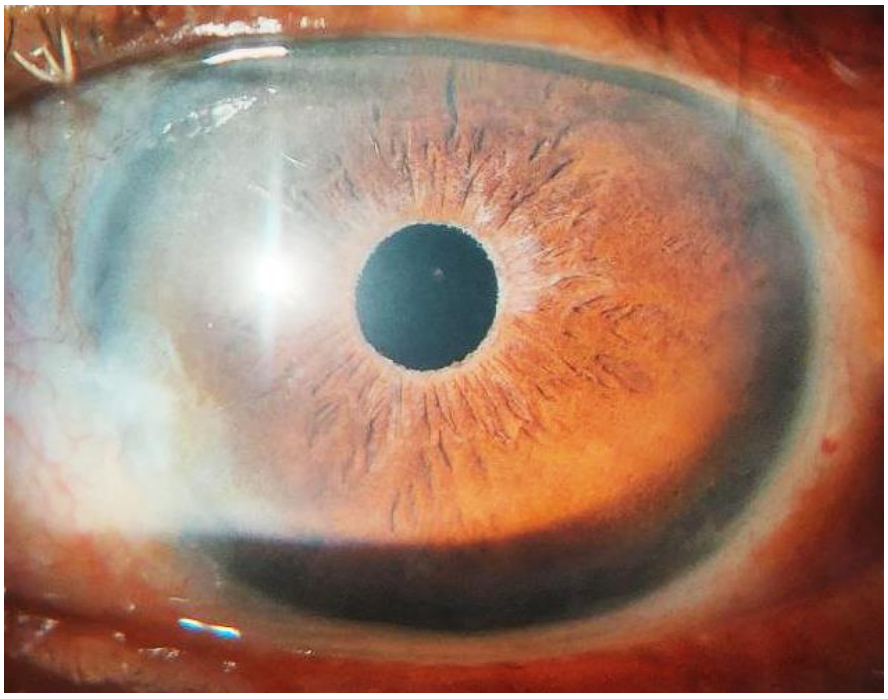

Figure 11: Post-cataract surgery aphakia in a severe PEX with iris atrophy.

Appendix V

Master Chart

Key for Master Chart:

Abbreviations	Full expansion
PEX	Pseudoexfoliation
ECG	Electrocardiogram
CAD	Coronary artery disease
CRP	C reactive protein
HDL	High-density lipoprotein
LDL	Low-density lipoprotein
VLDL	Very low-density lipoprotein
Total chol	Total cholesterol
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
FBS	Fasting blood sugar
PPBS	Post-prandial blood sugar
TG	Triglyceride
BE	Both eyes
RE	Right eye
LE	Left eye

Case No.	Name	Age	Sex	ECG	FBS	PPBS	LDL	HDL	VLDL	TOTAL CHOL	CRP	TG	SBP	DBP	Grading of PXF	PXF
1	Rantvabai Bapur Kari	72	2	1	82	93	105	78	26	209	1	128	148	90	2	BE
2	Gurappa Aralchandi	70	1	2	130	132	67	61	25	153	1	126	160	100	3	BE
3	Nagubai Polannavar	72	2	2	88	94	61	51	16	128	1	80	130	90	1	BE
4	Chandrashekhar Soddi	80	1	2	122	91	78	52	19	149	2	94	150	90	1	LE
5	Shantavva Hiremath	60	2	1	88	138	149	41	25	215	1	123	138	88	1	LE
6	Basappa Meldapur	70	1	1	133	174	115	32	12	159	1	58	146	106	3	BE
7	Basappa Talawar	75	1	1	89	88	78	32	26	136	1	130	126	82	1	BE
8	Shrikanath Ambiger	67	1	4	76	99	74	56	16	146	1	78	140	80	1	BE
9	Gangawwa Hitanalli	70	2	5	89	110	117	45	35	197	1	177	150	90	2	RE
10	Shamala Doddamani	55	2	4	109	99	120	65	30	215	1	148	160	100	3	BE
11	Hanamanth Nayak	70	1	1	87	79	60	59	17	136	1	85	134	90	2	BE
12	Mallamma Madar	70	2	4	93	92	122	56	18	196	1	89	160	100	1	RE
13	Bhimavva Madar	72	2	4	91	84	114	48	18	174	1	92	150	100	2	BE
14	Sumitra Kumbar	50	2	1	109	137	82	51	35	168	2	173	140	80	1	BE
15	Motibai Lamani	80	2	4	98	99	117	39	23	179	1	115	150	90	2	BE
16	Vittol Badaladinni	80	1	1	81	182	99	44	11	154	1	57	160	110	3	BE
17	Sahebngoud Biradar	56	1	1	94	152	92	48	17	157	1	87	138	90	1	RE
18	Kashimsab Kazi	66	1	5	92	107	50	49	6	105	1	30	160	100	2	BE
19	Davalsab Mulla	77	1	5	89	152	84	47	17	148	2	83	160	100	2	BE
20	Danappa Solapur	79	1	1	98	103	64	18	40	122	1	202	120	80	3	BE
21	Kantappa Hatti	60	1	2	85	91	73	38	24	135	1	118	160	90	2	LE
22	Suryakant Hadalgi	60	1	1	113	141	141	60	11	212	1	57	140	80	1	BE
23	Hiragappa Pujari	72	1	4	75	102	71	60	15	60	1	75	130	80	1	BE
24	Kasappa Hipparagi	75	1	1	95	95	100	31	19	150	1	94	140	80	1	BE
25	Irappa Alamel	75	1	2	87	70	106	32	22	160	1	109	150	100	3	BE
26	Basamma Badiger	61	2	2	100	115	26	87	46	159	1	46	150	110	3	BE
27	Havalappa Masiminal	75	1	1	116	116	93	37	57	187	1	187	130	84	1	BE
28	Nagavva Hosamani	72	2	1	83	100	94	54	21	169	1	103	128	80	1	BE
29	Rasulsab Koti	65	1	1	88	108	120	50	16	186	1	78	156	112	3	BE
30	Mallappa Awati	72	1	3	113	168	87	40	29	156	1	147	130	80	1	BE
31	Pandu Rathod	75	1	1	120	211	127	45	10	182	2	49	154	90	3	BE
32	Bhimashankar Salotagi	62	1	3	92	100	132	36	51	219	1	257	154	90	3	BE
33	Bhashasab Ankalagi	75	1	1	96	95	152	51	27	230	2	133	124	96	2	BE
34	Bibibai Chavan	75	2	2	119	122	89	37	16	142	1	81	142	90	2	BE
35	Nimbewwa layappa Walikar	65	2	1	81	69	127	43	19	189	1	94	130	70	1	BE
36	Muktamsab Mulla	80	1	4	70	86	102	62	34	198	1	172	156	100	3	BE
37	Basanna Pujari	84	1	3	98	72	106	33	47	186	1	233	140	80	1	BE
38	Mansingh Pawar	80	1	4	92	79	73	47	15	135	1	76	120	80	1	BE

RE CATARACT	LE CATARACT	HYPERTENSION	DIABETES MELLITUS	CAD	STROKE	OCULAR COMPLICATIONS	INTRAOPERATIVE COMPLICATIONS
3	4	1	2	2	2	1	1 and 3
1	4	2	2	2	2	1	1
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1	5	1	2	2	2	2	1 and 2
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1	2	2	2	2	2	1	3
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39	Laxmibai Benal	50	2	5	88	104	121	37	24	182	1	118	150	90	3	BE
40	Ballappa Walikar	60	1	3	95	91	187	49	13	152	1	63	140	80	2	BE
41	Shivappa Gonal	60	1	1	74	142	85	29	15	129	1	77	128	80	1	BE
42	Durgawwa Madar	70	2	5	106	184	91	67	20	178	1	98	140	80	1	BE
43	Shivappa Daneevar	66	1	3	87	100	92	27	16	135	1	79	144	86	2	BE
44	Mallappa Miragi	74	1	5	129	124	86	32	50	168	1	248	152	94	3	BE
45	Gurubai Chalawadi	70	2	1	151	162	159	48	28	48	1	138	130	80	1	BE
46	Parvati Gugihal	72	2	1	107	116	134	81	24	239	1	121	130	82	1	BE
47	Siddappa Javali	65	1	1	94	148	116	38	24	178	1	120	130	80	1	BE
48	Neelawwa Teli	70	2	1	148	257	184	55	184	295	1	278	150	100	3	BE
49	Beeranna Nandaragi	65	1	1	100	111	136	38	47	221	1	233	120	80	1	BE
50	Revabai Benakanalli	85	2	1	93	100	101	48	28	177	1	140	140	90	2	BE
51	Sayawwa Chalwadi	50	2	1	90	93	127	40	24	191	1	122	140	80	2	BE
52	Jairabai	75	2	2	93	108	79	61	16	156	1	82	130	84	1	RE
53	Mallappa Biradar	70	1	1	79	125	96	125	55	190	1	273	126	84	1	BE
54	Shivagond Pujari	65	1	1	104	153	77	64	16	157	1	81	122	90	1	BE
55	Basappa Kalegab	75	1	3	106	105	99	36	27	162	1	134	164	98	3	BE
56	Neelamma Pujari	60	2	5	88	82	94	34	21	149	1	107	160	98	3	BE
57	Sangavva Akkiwad	68	2	1	77	86	36	36	21	150	1	104	120	70	1	BE
58	Umalabai chavan	74	2	4	147	114	130	37	35	202	1	175	148	100	3	BE
59	Chaya Ramesh Kadam	61	2	5	119	88	116	41	16	173	1	79	138	94	2	BE
60	Basalingappa	70	1	2	87	168	51	39	8	98	1	42	140	92	1	BE
61	Hiragavva Pujari	68	2	1	89	113	137	44	27	208	1	135	130	70	1	BE
62	Basavaraj Pujari	69	1	1	94	101	103	40	26	169	1	132	120	70	1	BE
63	Siddanna B Kumbar	65	1	1	95	89	101	48	17	166	1	86	138	82	2	BE
64	Ram Ningappa Madar	80	1	1	67	81	210	92	21	323	1	107	120	84	1	BE
65	Lakappa Ramappa Talawar	67	1	1	142	147	142	50	30	222	1	151	130	90	2	BE
66	Dasagirsab Kashimsab Mokashi	72	1	2	111	104	75	50	15	140	1	73	140	80	3	BE
67	Ambawwa Kanteppa Harijan	65	2	1	91	155	95	42	16	153	1	80	130	80	2	BE
68	Siddawwa Anandappa Pujari	67	2	5	92	154	108	36	15	159	1	76	150	100	3	BE
69	Shantabai Chavan	65	2	1	91	128	139	62	21	222	1	104	128	88	2	BE
70	Hulagappa Basappa	65	1	1	91	78	115	42	26	183	1	130	136	92	2	BE
71	Dundappa Biradar	72	1	1	92	128	74	25	33	132	1	166	140	100	3	BE
72	Shantappa Dasma	65	1	2	86	71	149	33	29	209	1	143	110	72	1	BE
73	Imanni Korwar	70	2	5	111	95	83	36	30	149	1	151	150	100	3	BE
74	Kashimsab Mummanager	72	1	1	96	110	61	28	38	127	1	188	130	80	2	BE
75	Murageppa Minajagi	75	1	3	90	140	87	29	29	145	1	147	152	110	3	BE
76	Avanna Basappa Badenur	60	1	1	83	107	154	52	21	227	1	103	144	92	2	BE

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2	4	1	1	2	2	1	1 and 2
1	1	2	2	2	2	1	1 and 4
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2	2	2	2	2	2	1	1
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77	Ramanagouda Tippanagouda Biradar	75	1	1	86	131	49	34	12	95	1	60	110	66	1	BE
78	Neelabai kamble	70	2	1	200	294	79	40	11	130	1	54	140	80	2	BE
79	Mallamma Bandari	50	2	1	228	246	82	56	16	154	1	197	148	92	2	BE
80	Shivamma Hanjagi	70	2	1	230	237	74	37	37	148	1	85	120	88	1	BE
81	Irawwa Ingaleshwar	60	2	3	225	270	71	31	75	177	1	76	150	88	3	BE
82	Gundawwa Madrikar	74	2	1	148	281	47	29	84	160	1	419	152	110	3	BE
83	Gourabai Aiholi	60	2	1	96	111	74	28	29	131	1	144	138	94	2	BE
84	Nagappa Kattimani	52	1	5	90	130	53	33	14	100	1	71	166	110	3	BE
85	Shankar Nagaral	65	1	1	72	87	88	36	31	155	1	154	150	90	2	BE
86	Gangabai Biradar	44	2	1	96	171	55	37	58	150	1	288	112	80	1	BE
87	Chandrabhaga Biradar	65	2	3	89	108	102	51	34	187	1	172	120	78	2	BE
88	Laxmibai Bilebhavi	70	2	1	70	136	138	54	40	232	1	198	140	90	2	BE
89	Govind Rathod	61	1	2	77	190	146	41	40	227	1	200	138	96	2	BE
90	Shantappa Bhoyar	70	1	1	85	150	169	61	19	249	1	96	140	80	2	BE
91	Siddanna Khadi	65	1	1	118	136	158	52	26	236	2	132	144	100	3	LE
92	Shivanna Nadvinmani	85	1	4	84	147	155	42	36	233	2	179	152	112	3	BE
93	Basamma Biradar	66	2	1	116	152	124	48	27	199	2	136	148	92	3	BE
94	Kasanu Kasu Rathod	70	1	3	88	132	127	31	25	183	1	124	140	92	2	LE
95	Shivappa Jogi	82	1	1	76	132	83	46	15	144	1	74	150	110	3	BE
96	Shantabai Rajput	67	2	3	80	93	89	46	29	164	2	146	144	100	2	LE
97	Lagamavva Jankar	70	2	1	70	101	114	35	30	179	1	148	130	80	2	BE
98	Lalasab Mulla	60	1	5	100	110	125	50	18	193	1	91	158	100	1	BE
99	Rajesab Kudargond	65	1	2	114	132	57	36	28	121	1	141	130	100	2	BE
100	Shivangouda	65	1	1	93	189	93	49	29	171	1	144	150	110	2	BE
101	Yamanavva Nalikar	83	2	3	135	225	93	39	16	148	1	82	148	100	3	BE
102	Fulabai Hosamani	72	2	1	87	93	195	45	43	283	1	216	136	88	1	BE
103	Dundappa Naikodi	79	1	1	131	175	52	57	11	120	1	57	156	116	2	BE
104	Akbar	83	1	4	235	270	65	27	19	111	2	93	144	96	2	BE
105	Hanamanth Guled	75	1	2	86	112	124	56	17	197	1	85	142	90	2	BE
106	Saraswati Honakore	70	2	3	86	190	88	89	38	215	1	190	140	82	2	BE
107	Kesu Jadhav	82	1	1	133	189	108	41	45	194	1	226	150	112	3	BE
108	Muddamma Gurikar	78	2	1	96	123	117	37	14	168	1	69	138	98	2	LE
109	Hanamanth Kesapur	76	1	1	130	203	144	37	73	254	1	366	120	80	1	BE
110	Madivalappa Totada	70	1	5	96	142	93	34	25	152	1	123	142	84	2	LE
111	Halevva Hadagali	70	2	2	97	141	93	34	21	148	1	120	144	110	3	BE
112	Chandrabhaga Kumbar	70	2	3	109	152	93	41	64	198	1	136	136	70	2	BE
113	Boramma Sajjan	65	2	4	101	142	100	28	73	201	1	148	148	96	2	BE
114	Sarubai Lad	60	2	1	136	186	128	20	71	219	1	156	146	92	2	BE

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2	4	2	2	2	2	2	1 and 3

Appendix VI

Plagiarism report

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Summary

References

1. Lindberg JG. Clinical Investigations on Depigmentation of the Pupillary Border and Translucency of the Iris in Cataract Cases and in Normal Eyes of Old Persons 1917. https://shorturl.at/pz8gZ

2. The History of Exfoliation Syndrome. Asia-Pacific Journal of Ophthalmology. 2019; https://doi.org/10.22608/APO.2018226

3. Schlotzer-Schrehardt U, Naumann GO. Ocular and systemic pseudoexfoliation syndrome. Am J Ophthalmol. 2006;141(5):921–37. https://doi.org/10.1016/j.ajo.2006.01.047

4. Patil A, Swiston C, Wallace RT, et al. Exfoliation Syndrome and Exfoliation Glaucoma in the Navajo Nation. Vision. 2022 Oct 3;6(4):61. https://doi.org/10.3390/vision6040061

5. Mitchell P. The Relationship Between Glaucoma and Pseudoexfoliation. Archives of Ophthalmology. 1999 Oct 1;117(10):1319. https://doi.org/10.1001/archopht.117.10.1319

6. Schlotzer-Schrehardt U. Genetics and genomics of pseudoexfoliation syndrome/glaucoma. Middle East Afr J Ophthalmol. 2011;18(1):30. https://doi.org/10.4103/0974-9233.75882

7. Thorleifsson G, Magnusson KP, Sulem P, et al. Common Sequence Variants in the *LOXL1* Gene Confer Susceptibility to Exfoliation Glaucoma. Science (1979). 2007 Sep 7;317(5843):1397–400. https://doi.org/10.1126/science.1146554

8. Chen H, Chen LJ, Zhang M, et al. Ethnicity-based subgroup meta-analysis of the association of LOXL1 polymorphisms with glaucoma. Mol Vis. 2010 Feb 6;16:167–77. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2817013/

9. Krumbiegel M, Pasutto F, Mardin CY, et al. Exploring Functional Candidate Genes for Genetic Association in German Patients with Pseudoexfoliation Syndrome and Pseudoexfoliation Glaucoma. Investigative Opthalmology & Visual Science. 2009 Jun 1;50(6):2796. https://doi.org/10.1167/iovs.08-2339

10. Morris J, Myer C, Cornet T, et al. Proteomics of pseudoexfoliation materials in the anterior eye segment. In 2021. p. 271–90. https://doi.org/10.1016/bs.apcsb.2021.03.004

11. Sharma S, Chataway T, Klebe S, et al. Novel protein constituents of pathological ocular pseudoexfoliation syndrome deposits identified with mass spectrometry. Mol Vis. 2018;24:801–17. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6334984/

12. Zenkel M, Lewczuk P, Jünemann A, et al. Proinflammatory Cytokines Are Involved in the Initiation of the Abnormal Matrix Process in Pseudoexfoliation Syndrome/Glaucoma. Am J Pathol. 2010 Jun;176(6):2868–79. https://doi.org/10.2353/ajpath.2010.090914

13. Schlötzer-Schrehardt UM. Pseudoexfoliation Syndrome Ocular Manifestation of a Systemic Disorder? Archives of Ophthalmology. 1992 Dec 1;110(12):1752. https://doi.org/10.1001/archopht.1992.01080240092038

14. Streeten BW. Pseudoexfoliative Fibrillopathy in Visceral Organs of a Patient With Pseudoexfoliation Syndrome. Archives of Ophthalmology. 1992 Dec 1;110(12):1757. https://doi.org/10.1001/archopht.1992.01080240097039

15. Andrikopoulos GK, Mela EK, Georgakopoulos CD, et al. Pseudoexfoliation syndrome prevalence in Greek patients with cataract and its association to glaucoma and coronary artery disease. Eye. 2009 Feb 12;23(2):442–7. https://doi.org/10.1038/sj.eye.6702992

16. Mocan MC, Dikmetas O, Irkec M. Serum C-reactive protein levels in exfoliation syndrome and exfoliative glaucoma. Eye. 2011 Oct 8;25(10):1383–4. https://doi.org/10.1038/eye.2011.166

17. Gonen KA, Gonen T, Gumus B. Renal artery stenosis and abdominal aorta aneurysm in patients with pseudoexfoliation syndrome. Eye (Lond). 2013 Jun;27(6):735–41. https://doi.org/10.1038/eye.2013.56

18. Sorkhabi R, Ghorbanihaghjo A, Ahoor M, et al. High-sensitivity C-reactive Protein and Tumor Necrosis Factor Alpha in Pseudoexfoliation Syndrome. Oman Med J. 2013 Jan;28(1):16–9. https://doi.org/10.5001/omj.2013.04

19. Vardhan S A, Haripriya A, Ratukondla B, et al. Association of Pseudoexfoliation With Systemic Vascular Diseases in a South Indian Population. JAMA Ophthalmol. 2017 Apr 1;135(4):348. https://doi.org/10.1001/jamaophthalmol.2017.0064

20. Kurtul BE, Kurtul A, Altiaylik Ozer P, et al. Serum Lipid Levels in Pseudoexfoliation Syndrome. Semin Ophthalmol. 2017 May 4;32(3):281–4. https://doi.org/10.3109/08820538.2015.1068341

21. Chellakumar V, Rashmi P, Balakrishnan M. Cardiovascular Diseases Associated With Pseudoexfoliation Syndrome – A Prospective Cross-Sectional Study. Asian Journal of Pharmaceutical and Clinical Research. 2019 Nov 27;21–3. https://doi.org/10.22159/ajpcr.2020.v13i1.36177

22. Pooja H V., Venkate Gowda HT, Subhashchandra. Pseudoexfoliative cataract with associated systemic disorders. Indian Journal of Clinical and Experimental Ophthalmology. 2020;6(1):61–2. https://doi.org/10.18231/j.ijceo.2020.013

23. Scharfenberg E, Rauscher FG, Meier P, et al. Pseudoexfoliation syndrome: analysis of systemic comorbidities of 325 PEX-positive patients compared with 911 PEX-negative patients. Graefe's Archive for Clinical and Experimental Ophthalmology. 2019 Nov 16;257(11):2471–80. https://doi.org/10.1007/s00417-019-04438-4

24. Rumelaitienė U, Žaliūnienė D, Špečkauskas M, et al. Link of ocular pseudoexfoliation syndrome and vascular system changes: results from 10-year follow-up study. Int Ophthalmol.2020Apr19;40(4):957–66.https://doi.org/10.1007/s10792-019-01262-x

25. Axenfeld T. Uber besondere formen von irisatrophie, besonders die hyaline degeneration des pupillarsaumes und die pupillare pigmentatrophie des irishinterblattes. 1911; https://doi.org/10.22608/APO.2018226

26. Fuchs E. Beiträge zur normalen Anatomie der menschlichen Iris. Albrecht Von Graefes Arch Ophthalmol. 1885 Sep;31(3):39–86. https://austriaca.at/0xc1aa5576%200x003ca346.pdf

27. Tarkkanen A. Exfoliation Syndrome: A Historical Perspective. J Glaucoma. 2018 Jul;27(Supplement 1):S1–3. https://doi.org/10.1097/IJG.0000000000000901

28. Ashton N. In discussion to Gifford. A clinical and pathologic study of exfoliation of the lens capsule. Trans Amer Ophthalmol Soc. 1957; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1312671/

29. Elschnig A. A Detachment of the zonular lamellae in glassblowers. Klin Monatsbl Augenheilkd. 1922;(69):732–4. https://doi.org/10.4103/ijo.IJO_1631_19

30. Dvorak-Theobald G. Pseudo-exfoliation of the lens capsule. Relation to “true” exfoliation of the lens capsule as reported in the literature and role in the production of glaucoma capsulocuticulare. Am J Ophthalmol. 1954; https://doi.org/10.1016/j.ajo.2018.02.018

31. Young AL. The prevalence of pseudoexfoliation syndrome in Chinese people. British Journal of Ophthalmology. 2004 Feb 1;88(2):193–5. https://doi.org/10.1136/bjo.2003.021816

32. Melese EK, Shibeshi MA, Sherief ST. Prevalence of Pseudoexfoliation Among Adults and Its Related Ophthalmic Variables in Southern Ethiopia: A Cross-Sectional Study. Clinical Ophthalmology. 2022 Nov;Volume 16:3951–8. https://doi.org/10.2147/OPTH.S391290

33. Forsius H. Prevalence of pseudoexfoliation of the lens in Finns, Lapps, Icelanders, Eskimos, and Russians. Trans Ophthalmol Soc U K. 1979;(99):296–8. https://pubmed.ncbi.nlm.nih.gov/298430/

34. Sood NN. Prevalence of pseudoexfoliation of the lens capsule in India. Acta Ophthalmol. 1968 Apr 27;46(2):211–4. https://doi.org/10.1111/j.1755-3768.1968.tb05179.x

35. Cashwell LF, Shields MB. Exfoliation syndrome in the southeastern United States I.Prevalence in open –angle glaucoma and non- glaucoma Populations. Acta Ophthalmol. 1988;(184):99–102. https://doi.org/10.1001/archopht.1988.01060130361021

36. Taylor HR, Hollows FC, Moran D. Pseudoexfoliation of the lens in Australian Aborigines. British Journal of Ophthalmology. 1977 Jul 1;61(7):473–5. https://doi.org/10.1136/bjo.61.7.473

37. Faulkner HW. Pseudo-Exfoliation of the Lens Among the Navajo Indians. Am J Ophthalmol. 1971 Jul;72(1):206–7. https://doi.org/10.1016/0002-9394(71)91616-3

38. Irvine R. . Arch. Ophthal. 1940. p. 139–60.

39. Thomas RM, Paul PM, Muliyil JD. Glaucoma in India. Journal of Glaucoma . 2003 Feb;(12):81–7. https://doi.org/10.1097/00061198-200302000-00016

40. Vijayalakshmi V, Desai S, Prasanna N, et al. Pseudoexfoliation Syndrome: Prevalence In South Indian Population. . Int J Med Sci Clin Invent [Internet]. 2015 [cited 2023 Dec 3];2(3):766–71. Available from: https://shorturl.at/N0h5Q

41. Allingham R, Damji K, Freedman S. Shields Textbook of Glaucoma. 6th ed. Lippincott Williams & Wilkins; 2012. http://dx.doi.org/10.1097/IJG.0b013e31822f4641

42. Tomczyk-Socha M, Tomczak W, Winkler-Lach W, et al. Pseudoexfoliation Syndrome—Clinical Characteristics of Most Common Cause of Secondary Glaucoma. Vol. 12, Journal of Clinical Medicine. Multidisciplinary Digital Publishing Institute (MDPI); 2023. https://doi.org/10.3390/jcm12103580

43. Ritch R. Ocular Findings in Exfoliation Syndrome. J Glaucoma. 2018 Jul;27(Supplement 1):S67–71. https://doi.org/10.1097/IJG.0000000000000986

44. Sampaolesi R, Zarate J, Croxato O. The chamber angle in exfoliation syndrome. Acta Ophthalmol. 1988 Mar 28;66(S184):48–53. https://doi.org/10.1111/j.1755-3768.1988.tb02628.x

45. Detorakis E, Bontzos G, Drakonaki E, et al. Changes in peri-ocular anatomy and physiology in pseudoexfoliation syndrome (Review). Exp Ther Med. 2021 Apr 19;21(6):650. https://doi.org/10.3892/etm.2021.10082

46. Irkec M. Clinical Features of Exfoliative Glaucoma w Exfoliation Syndrome and Exfoliative Glaucoma. PubliComm: Savona. 2015; https://doi.org/10.3390/jcm12103580

47. Ariga M, Nivean M, Utkarsha P. Pseudoexfoliation syndrome. Vol. 7, Journal of Current Glaucoma Practice. Jaypee Brothers Medical Publishers (P) Ltd; 2013. p. 118–20. https://doi.org/10.5005/jp-journals-10008-1148

48. Konstas AGP. Diurnal Intraocular Pressure in Untreated Exfoliation and Primary Open-angle Glaucoma. Archives of Ophthalmology. 1997 Feb 1;115(2):182. https://doi.org/10.1001/archopht.1997.01100150184006

49. Tezel G, Tezel TH. The comparative analysis of optic disc damage in exfoliative glaucoma. Acta Ophthalmol. 1993 Dec 27;71(6):744–50. https://doi.org/10.1111/j.1755-3768.1993.tb08594.x

50. Iwanejko M, Turno-Kręcicka A, Tomczyk-Socha M, et al. Evaluation of the anterior chamber angle in pseudoexfoliation syndrome. Advances in Clinical and Experimental Medicine. 2017 Aug 31;26(5):795–801. https://doi.org/10.17219/acem/64023

51. Teus MA, Castejón MA, Calvo MA, et al. Intraocular pressure as a risk factor for visual field loss in pseudoexfoliative and in primary open-angle glaucoma. Ophthalmology. 1998 Dec;105(12):2225–30. https://doi.org/10.1016/S0161-6420(98)91220-9

52. Çerik İB, Dindaş F, Yalınbaş Yeter D. Pseudoexfoliation syndrome: Are the eyes the mirror of the heart? Echocardiography. 2021 Apr 18;38(4):604–11. https://doi.org/10.1111/echo.15031

53. Thatte U, Puri K, Suresh K, Gogtay N. Declaration of Helsinki, 2008: Implications for stakeholders in research. J Postgrad Med. 2009;55(2):131. https://doi.org/10.4103/0022-3859.52846

54. Aoki T, Kitazawa K, Inatomi T, et al. Risk Factors for Corneal Endothelial Cell Loss in Patients with Pseudoexfoliation Syndrome. Sci Rep. 2020 Apr 29;10(1):7260. https://doi.org/10.1038/s41598-020-64126-w

55. French D, Margo C, Harman L. Ocular pseudoexfoliation and cardiovascular disease: A national cross-section comparison study. N Am J Med Sci. 2012;4(10):468. https://doi.org/10.4103/1947-2714.101987

56. Warjri GB, Das AV, Senthil S. Clinical profile and demographic distribution of pseudoexfoliation syndrome: An electronic medical record-driven big data analytics from an eye care network in India. Indian J Ophthalmol. 2023 Jul;71(7):2746–55. https://doi.org/10.4103/IJO.IJO_2619_22

57. Aristimuño NI, Agirretxe IR, Blanco RSV, et al. Comparison of Cardiovascular Risk and Events among Spanish Patients with and without Ocular Pseudoexfoliation. J Clin Med. 2022 Apr 1;11(8). https://doi.org/10.3390/jcm11082153

58. Akarsu C, Ünal B. Cerebral hemodynamics in patients with pseudoexfoliation glaucoma. Eye. 2005;19(12):1297–300. https://doi.org/10.1038/sj.eye.6701776

59. Akritidou F, Karachrysaphi S, Papamitsou T, et al. Pseudoexfoliation syndrome in diabetic patients: atransmission electron microscopy study of anterior lens epithelial

cells. Rom J Ophthalmol. 2021 Apr 15;65(1):38–45. https://doi.org/10.22336/rjo.2021.8

60. Yu M, Hwang HH, Wiggs JL, et al. Association between Diabetes and Exfoliation Syndrome. Ophthalmology Science. 2024 May;4(3):100436. https://doi.org/10.1016/j.xops.2023.100436

61. Mitchell P, Wang JJ, Smith W. Association of Pseudoexfoliation Syndrome With Increased Vascular Risk. Am J Ophthalmol. 1997 Nov;124(5):685–7. https://doi.org/10.1016/s0002-9394(14)70908-0

62. Citirik M, Acaroglu G, Batman C, et al. A possible link between the pseudoexfoliation syndrome and coronary artery disease. Eye. 2007 Jan 24;21(1):11–5. https://doi.org/10.1038/sj.eye.6702177

63. Mirza E. Atherogenic indices in pseudoexfoliation syndrome. Eye. 2019 Dec 5;33(12):1911–5. https://doi.org/10.1038/s41433-019-0506-z

64. Khataminia G, Saadatfar A, Gorgi A, et al. Plasma Lipid Levels in Patients with Cataract, with and without Pseudoexfoliation Syndrome. Jentashapir Journal of Health Research. 2016 Oct 19;7(5). https://doi.org/10.17795/jjhr-34338

65. Lesiewska H, Łukaszewska-Smyk A, Odrowąż-Sypniewska G, et al. Chosen Vascular Risk Markers in Pseudoexfoliation Syndrome: An Age-Related Disorder. J Ophthalmol. 2017;2017:1–4. https://doi.org/10.1167/iovs.63.9.15

66. Abay RN, Katipoğlu Z. The correlation between pseudoexfoliation syndrome and the Triglyceride-Glucose index. Graefe's Archive for Clinical and Experimental Ophthalmology. 2022 Dec 20;260(12):3903–8. https://doi.org/10.1007/s00417-022-05737-z

67. Egemen Erkayhan G, Dogan S. Cataract Surgery and Possible Complications in Patients with Pseudoexfoliation Syndrome. Eurasian J Med. 2017 Mar 31;49(1):22–5. https://doi.org/10.5152/eurasianjmed.2016.0060

68. Thevi T, Abas A. Intraoperative and postoperative complications of cataract surgery in eyes with pseudoexfoliation – An 8-year analysis. Oman J Ophthalmol. 2019;12(3):160. https://doi.org/10.4103/ojo.OJO_238_2018

69. Yüksel N, Pirhan D, Altntaş Ö, et al. Systemic High-sensitivity C-reactive Protein Level in Pseudoexfoliation Syndrome and Pseudoexfoliation Glaucoma. J Glaucoma. 2010 Aug;19(6):373–6. https://doi.org/10.1097/IJG.0b013e3181bdb570

70. Lesiewska H, Malukiewicz G, Mańkowska-Cyl A, et al. Lipids and C-reactive protein as vascular risk markers in pseudoexfoliation syndrome. Acta Ophthalmol. 2016 Aug 8;94(5). https://doi.org/10.1111/aos.12883

71. Kymionis GD, Kankariya VP, Kontadakis GA. Long-term presence of metallic particles in the DSAEK interface. Eye. 2011 Oct 8;25(10):1382–3. https://doi.org/10.1038/eye.2011.165