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Original Research Article

# Study of prevalence and systemic association of pseudoexfoliative syndrome in tertiary care centre of India

**Sania Rajesh Gulwani[1]*, Kamini Prajapati[1]**

[1]*Dept. of Ophthalmology, M & J Institute of Ophthalmolog (BJ Medical College), Ahmedabad, Gujarat, India*

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ABSTRACT

**Background**: Pseudoexfoliation syndrome (PEX) is characterized by the deposition of fibrillar material in ocular and extraocular tissues. It originates from various ocular structures such as the lens capsule, ciliary body, corneal endothelium, zonules, and iris, with deposits found in extraocular tissues like liver, lung, kidney, gall bladder and meninges. The study provides valuable insights into the occurrence and impact of PEX on both ocular and systemic health, contributing to a comprehensive understanding of this condition.
**Materials and Methods**: It is a hospital-based prospective observational cross-sectional study. 200 eyes were examined and classified based on the presence of features of PEX syndrome with or without glaucomatous change in relation to any systemic conditions if present. A comprehensive history,assessment of best-corrected visual acuity and anterior segment evaluation was conducted using slit lamp biomicroscopy. Detailed glaucoma examination was done using Ultrasonic pachymeter (corneal thickness, Goldman applanation tonometer (intraocular pressure), Zeiss 4 mirror gonioscopy (angles examination), Octopus automated static perimeter (900) for Visual field testing and optic nerve head evaluation using slit lamp biomicroscopy with a 90D lens. Furthermore, routine blood investigations, diabetic profile, ECG, 2D echo, chest X-ray, thyroid profile, serum immune profile, audiometry, and the collection of CT and MRI imaging reports, if available with patient, were included in the overall assessment.
**Results**: Over the span of two years, 2489 patients were screened and PEX syndrome was found in 100 patients (200 eyes) making it 4% prevalent, revealing a peak incidence in the 61-70 age group, with female predominance being 57%. 50 eyes (26%)were diagnosed with angle closure glaucoma, 28 eyes (14%) with open angle glaucoma,72 eyes (36%) were glaucoma suspects and rest 50 eyes (26%) did not have any glaucomatous changes.Systemic associations ranked as follows: Hypertension (76%) > Diabetes Mellitus (62%) > Sensorineural Hearing Loss (38%) > Ischemic Cardiac Condition (34%)>Alzheimer's Disease(14%) > Bronchial Asthma (7%) >thyroid issues (6%)>HIV(3%), and prostate cancer (1%).
**Conclusion**: The conclusion underscored PEX as a definite risk factor for glaucoma development, consolidating insights into demographic patterns,ocular complications,and systemic associations in PEX patients.



## 1. Introduction

Pseudoexfoliation syndrome (PEX) is characterized by the deposition of fibrillar material in ocular and extraocular tissues, primarily affecting the elderly and exhibiting variability across geographic regions and ethnicities.[1] This syndrome poses an increased risk of cataract and glaucoma, potentially complicating cataract surgery and leading to late intraocular lens displacement.[2] The fibrillar material originates from various ocular structures such as the lens capsule, ciliary body, corneal endothelium, zonules, and iris, with deposits also found in extraocular tissues like

* *Corresponding author*.
*E-mail address*: saniagulwani007@gmail.com (S. R. Gulwani).

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the liver, lung, kidney, gall bladder, and meninges.[3,4] Despite being composed of non-collagenous proteins, the exact origin of the material remains elusive, resembling zonular elastic microfibrils and suggesting an underlying elastosis process.[5] PEX may also be associated with lattice corneal degeneration and amyloid build-up. Diagnosis typically involves slit lamp examination, gonioscopy, pupillary dilation, and ultrasound biomicroscopy to assess lens subluxation or zonular changes. Iris fluorescein angiography is useful for detecting potential iris ischemia.[6] Diurnal intraocular pressure curve assessment is crucial for therapeutic management.[7]

The prevalence of glaucoma varies globally, with primary open-angle glaucoma (POAG) affecting approximately 2.2% of the world population, totaling 57.5 million individuals.[8] In Europe, 7.8 million people, constituting 2.51% of the population, suffer from POAG.[9] POAG is particularly prominent in the UK, affecting 2% of those over 40 and 10% over 75, predominantly among individuals of African and Caribbean descent. Primary angle-closure glaucoma (PACG) is less common, impacting 0.17% of those under 40, primarily individuals of East Asian descent.[10] Socioeconomic disparities and genetic/environmental factors contribute to regional and racial variations in glaucoma prevalence.[11] Notably, the IGBO tribe in Nigeria exhibits the highest glaucoma frequency, emphasizing potential genetic influences.[12] Black individuals experience earlier onset of POAG, being six times more likely than whites, while Mongolians and Burmese are more susceptible to PACG.[13] Glaucoma prevalence varies within ethnic groups based on the country of birth.[14]

Additionally, the global prevalence of pseudoexfoliative syndrome (PEX) ranges from 0.5% in those aged <60 to 15% in those aged >=60, with reports from India indicating prevalence between 1.87% and 13.5%.[15,16] Population-based studies in South India report PEX prevalence between 3.8% and 6% among individuals aged >40.[17] Age-related conditions such as macular degeneration, vascular issues, and obstructive sleep apnea are linked to glaucoma, as their prevalence increases with age.[18]

When compared to individuals with unilateral involvement, patients with bilateral PEX are generally older and have a higher prevalence of glaucoma or ocular hypertension. The deposition of pseudoexfoliative material, which obstructs the trabecular meshwork and raises IOP levels, has been generally cited as the cause of glaucoma. PEX can cause chronic open-angle glaucoma, angle-closure glaucoma, lens subluxation, blood-aqueous barrier impairment, and complications during cataract extraction, such as capsular rupture, zonular dialysis, and vitreous loss.[5] Although medical therapy typically has poor outcomes, a number of surgical methods have been suggested to more effectively treat this syndrome's clinical symptoms. PEX material deposits have been discovered in a number of extraocular regions in addition to the long-known intraocular manifestations, and they believe to represent a systemic mechanism linked to increased cardiovascular and cerebrovascular morbidity.

The pathogenetic theory of PEX as a form of stress-induced elastic microfibrillopathy is supported by molecular and biochemical data. Both hereditary and non-genetic variables are involved in the etiopathogenesis of PEX. The Lysyl-Oxidase-Like 1 (LOXL1) gene, which facilitates the cross-linking of elastin, has single-nucleotide polymorphisms (SNPS) in its coding area that have been identified as significant genetic risk factors for PEX syndrome and PEX glaucoma.

## 2. Materials and Methods

The study is a hospital-based prospective observational cross-sectional study conducted at the M and J Institute of Ophthalmology (government eye hospital), Civil Hospital, Ahmedabad, over a duration of two years from July 2020 to July 2022. The sample size comprises 200 eyes, and Ethical clearance was obtained from the Institutional Ethical Committee vide letter no 22/2021 dated: 03/02/2021 and informed written consent was taken from each patient before the surgery.

All findings were classified for both eyes, and patients were categorized based on the presence of features of Pseudoexfoliative syndrome with or without glaucomatous change in relation to any systemic conditions if present.

The study design and methods aim to comprehensively analyze the prevalence and occurrence of Pseudoexfoliation Syndrome and potential systemic associations, providing valuable insights into the disease's clinical and demographic characteristics. The data collection process for this study involved several steps. Firstly, patients were informed about the study, and written consent was obtained. A comprehensive history, encompassing present, past, family, and systemic aspects, was then documented. Visual acuity was evaluated using Snellen's and Jaeger charts, including the assessment of best-corrected visual acuity. Ultrasonic pachymetry was performed to determine central corneal thickness, Intraocular pressure was measured through Goldmann applanation tonometry, while anterior segment evaluation was conducted using slit lamp biomicroscopy and examination of anterior chamber angles was carried out using a Goldmann four mirror goniolens. Visual field testing utilized the Octopus automated static perimeter (900). After pupillary dilation, posterior segment evaluation with indirect ophthalmoscopy (20D lens), and optic nerve head evaluation using slit lamp biomicroscopy with a 90D lens were employed after dilating both eyes. Furthermore, routine blood investigations, diabetic profile, ECG, 2D echo, chest X-ray, serum PSA, thyroid profile, serum immune profile, audiometry, and the collection of CT and MRI

imaging reports, if available with patient, were included in the overall assessment.

## 3. Results

Over the span of two years, in glaucoma clinic 2489 patients were screened and psedoexfoliation syndrome was found in 100 patients (200 eyes) making it 4% prevalent. Out of 200 eyes 50 eyes (26%) were diagnosed with angle closure glaucoma, 28 eyes (14%) were diagnosed with open angle glaucoma, 72 eyes (36%) were glaucoma suspects and rest 50 eyes (26%) did not have any glaucomatous changes. Female predominance in glaucoma was found with 57%. The data presents the distribution of systemic illnesses among male and female participants, along with the overall totals expressed as percentages. Amongst total cases, maximum number of cases (40%) were from 61-70 year age group.(Table 1) Furthermore, 57% of cases being female and rest males.(Table 2) Amongst systemic illnesses, hypertension was found in 76 patients (76%) in which 33 patients (43.42%) were males and 43 (56.58%) were females. Diabetic mellitus was found in 62 patients (62%) in which 28 patients (45.16%) were males and 34 (54.84%) were females. Cardiac disease was found in 34 patients (34%) in which 11 patients (32.35%) were males and 23 (67.65%) were females. Sensory neural hearing loss was found in 38 patients (38%) in which 14 patients (36.84%) were males and 24 (63.16%) were females. Alzheimer's disease was found in 14 patients (14%) in which 2 patients (14.29%) were males and 12 (85.71%) were females. Bronchial asthma was found in 7 patients (7%) in which 5 patients (71.43%) were males and 2 (28.57%) were females. Prostate cancer was exclusive to males, with 1% of incidence among cases. HIV was found in 3 patients (3%) in which 1 patient (33.33%) were male and 2 (66.67%) were females. Thyroid issues was found in 6 patients (6%) in which 3 patients (50%) were males and 3 (50%) were females.(Table 3)

**Table 1:** Age group distribution

| Age (Years) | Number of Cases | Percentage |
|---|---|---|
| 31-40 | 6 | 6.0 |
| 41-50 | 12 | 12.0 |
| 51-60 | 32 | 32.0 |
| 61-70 | 40 | 40.0 |
| 71-80 | 10 | 10.0 |
| Total | 100 | 100.0 |

**Table 2:** Gender association

| Gender | Number of Cases | Percentage |
|---|---|---|
| Female | 57 | 57.0 |
| Male | 43 | 43.0 |
| Total | 100 | 100.0 |

**Figure 1:** PEX material over anterior lens capsule

## 4. Discussion

The observational study focused on analyzing 100 cases of pseudoexfoliation syndrome (PEX) in patients attending the outpatient department, aiming to explore various aspects, including clinical features, associations, and systemic implications. PEX is characterized by the deposition of fibrillar extracellular debris in intraocular (Figure 1) and extraocular tissues, more commonly observed in the elderly and varying across geographic regions and ethnicities.

In the study, the most common age group affected by PEX was found to be between 61-70 years, highlighting that PEX is predominantly a disease of the elderly population. The prevalence of bilateral PEX was higher than unilateral cases, suggesting that unilateral occurrences may progress to bilateral involvement over time. A comparative analysis with other studies revealed variations in mean age and laterality, emphasizing the need for a comprehensive understanding of the demographic aspects of PEX.

Amongst all cases 33% of them were diagnosed unilateral psedoexfoliation syndrome, whilst in 67% cases were bilateral at presentation.

The dataset provides a comprehensive view of the distribution of eyes among individuals studied for glaucoma. Out of the total 200 eyes examined, 50 eyes (26%) were identified as having angle closure glaucoma, a condition characterized by blocked drainage canals leading to increased eye pressure. Open-angle glaucoma, another common form of the disease where the drainage angle remains open but the trabecular meshwork becomes less efficient, was diagnosed in 28 eyes (14%). Additionally,

**Table 3:** Systemic illness

| Systemic Illness | Male | | Female | | Total | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| Hypertension | 33 | 43.42 | 43 | 56.58 | 76 | 100 |
| Diabetes Mellitus | 28 | 45.16 | 34 | 54.84 | 62 | 100 |
| Cardiac Disease | 11 | 32.35 | 23 | 67.65 | 34 | 100 |
| Sensory Neural Hearing Loss | 14 | 36.84 | 24 | 63.16 | 38 | 100 |
| Alzheimer's disease | 2 | 14.29 | 12 | 85.71 | 14 | 100 |
| Bronchial Asthma | 5 | 71.43 | 2 | 28.57 | 7 | 100 |
| Prostate Cancer | 1 | 100 | 0 | 0 | 1 | 100 |
| HIV | 1 | 33.33 | 2 | 66.67 | 3 | 100 |
| Thyroid | 3 | 50 | 3 | 50 | 6 | 100 |

72 eyes (36%) were classified as glaucoma suspects, indicating individuals with certain risk factors or early signs of glaucoma but without definitive diagnosis yet. This breakdown sheds light on the different types and stages of glaucoma within the study cohort, highlighting the importance of early detection and management to prevent vision loss associated with this progressive eye disease.

Glaucoma, a serious complication associated with PEX, was a focal point of investigation in the study. Among the examined cases, approximately 75% of PEX patients were found to have glaucoma (including suspects). Further categorization indicated that angle closure glaucoma was more prevalent than open-angle glaucoma in PEX patients. This finding provides valuable insights into the association between PEX and different types of glaucoma, contributing to a better understanding of the disease's impact on ocular health.

The study delved into specific challenges related to cataract management in PEX patients. It identified instances of poor pupillary dilatation, particularly following the administration of mydriatic agents. The study suggested that intrinsic degenerative changes occurring in the sphincter papillae in pseudoexfoliation syndrome could lead to secondary sphincter atrophy, resulting in decreased pupillary dilatation. This observation implies potential difficulties in cataract surgery among PEX patients, highlighting the importance of careful preoperative evaluation.

The systemic associations of PEX were thoroughly investigated in the study. Hypertension and cardiovascular disease were explored, revealing a positive correlation between these conditions and pseudoexfoliative syndrome. Specifically, 76 cases (43.42% male, 56.58% female) had hypertension, and 34 cases (32.35% male, 67.65% female) had cardiovascular disease. The study's findings contribute to the growing body of evidence linking PEX with various systemic diseases, shedding light on the potential broader health implications of this ocular condition. Insults to the vascular endothelium and smooth muscle function by PEX deposits have also been postulated as a mechanism for atherosclerosis and thrombus formation, which could lead to cardiac events. Higher levels of coronary risk markers, such as lipoprotein A, apolipoprotein A, and homocysteine, have also been previously reported in patients with PEX compared with control individuals without PEX, mainly as 60 parts of relatively small clinical studies. Higher levels of systemic homocysteine have been suggested as a possible reason for an increase in cardiovascular disease given that homocysteine, 35-40 an amino acid synthesized during methionine metabolism, is an independent risk factor for cardiovascular disease in some studies.

Diabetes mellitus (DM) was another systemic condition examined in the context of PEX. The study found that 63 cases (45.16% male, 58.84% female) out of 100 cases had DM, indicating a significant association between PEX and diabetes. This observation aligns with existing research suggesting a complex interplay between PEX and metabolic disorders, emphasizing the need for interdisciplinary collaboration in managing patients with these comorbidities.

Sensorineural hearing loss was investigated as a potential systemic association with PEX. The study identified 38 cases (36.84% male, 63.16% female) with sensorineural hearing loss, indicating a prevalence of this condition in individuals with pseudoexfoliative syndrome. The link between PEX and sensorineural hearing loss has been debated in the literature, with conflicting results in various studies. The present findings contribute to this ongoing discourse, adding more nuanced insights into the potential auditory implications of PEX.

Alzheimer's disease (AD) was explored as another systemic association with PEX. The study identified 14 cases (14.29% male, 85.71% female) with Alzheimer's disease among the examined PEX patients. This observation adds to the evolving understanding of PEX as a systemic condition that may share common features with neurodegenerative disorders. The association between PEX and AD has been a subject of interest, with previous research suggesting a potential link based on shared pathological mechanisms.

The study also considered several other systemic illnesses, such as bronchial asthma, HIV, anemia, and

hypothyroidism. However, no significant associations were found between these conditions and pseudoexfoliation syndrome. The lack of association suggests that the occurrence of PEX in conjunction with these specific systemic illnesses may be coincidental rather than indicative of a direct causal relationship.

In summary, the observational study on pseudoexfoliation syndrome provided a comprehensive analysis of its clinical features, associations, and systemic implications. The findings contribute to the existing body of knowledge surrounding PEX, offering valuable insights for clinicians, researchers, and healthcare professionals involved in the management of patients with this complex ocular condition. The study's multifaceted approach, encompassing demographic characteristics, glaucoma associations, challenges in cataract management, and systemic correlations, enhances our understanding of the broader impact of pseudoexfoliation syndrome on both ocular and systemic health.

## 5. Conclusion

The study on pseudoexfoliation syndrome (PEX) investigated 100 cases, revealing a peak incidence in the 61-70 age group, with a mean age of 63.71 years. Notably, 18% of cases occurred in individuals under 50. Bilateral PEX was more prevalent (67%) than unilateral cases, with females showing a higher predominance. Pseudoexfoliation glaucoma demonstrated a female predominance in both unilateral (60.60%) and bilateral (55.20%) cases.

The study extensively explored the systemic associations of Pseudoexfoliation syndrome (PEX), focusing on hypertension and cardiovascular disease. The findings revealed a positive correlation, with 43.42% of male and 56.58% of female participants having hypertension, and 32.35% of male and 67.65% of female participants having cardiovascular disease. These results contribute to the growing body of evidence linking PEX with systemic conditions, highlighting potential broader health implications.

Diabetes mellitus (DM) was also investigated, showing a significant association with PEX. Out of 100 cases, 45.16% were male, and 58.84% were female with DM, emphasizing the complex interplay between PEX and metabolic disorders. This underscores the importance of interdisciplinary collaboration in managing patients with these comorbidities.

Sensorineural hearing loss was explored as a potential systemic association with PEX, identifying 36.84% male and 63.16% female cases with this condition. The study contributes nuanced insights into the auditory implications of PEX, adding to the ongoing discourse on the debated link between PEX and sensorineural hearing loss.

Alzheimer's disease (AD) was examined as another systemic association, revealing 14.29% male and 85.71% female cases with AD among PEX patients. This supports the evolving understanding of PEX as a systemic condition sharing common features with neurodegenerative disorders, aligning with previous research suggesting a potential link based on shared pathological mechanisms.

Several other systemic illnesses, including bronchial asthma, HIV, anemia, and hypothyroidism, were considered, but no significant associations were found with PEX. The lack of association suggests that the co-occurrence of PEX with these specific systemic illnesses may be coincidental rather than indicative of a direct causal relationship.

Cataract incidence was high, with 71% having nuclear cataract, and 1.50% experiencing subluxated lens due to zonular weakness. Systemic associations ranked as follows: Hypertension > Diabetes Mellitus > Sensorineural Hearing Loss > Ischemic Cardiac Condition > Alzheimer's Disease > Bronchial Asthma. Incidental findings included thyroid issues (6 cases), HIV (3 cases), and prostate cancer (1 case).

The conclusion underscored PEX as a definite risk factor for glaucoma development, consolidating insights into demographic patterns, ocular complications, and systemic associations in PEX patients.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

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## Author's biography

**Sania Rajesh Gulwani,** Senior Resident

**Kamini Prajapati,** Associate Professor https://orcid.org/0009-0003-4768-3785

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