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**Original research article**

# Clinical spectrum of pseudo exfoliation syndrome; A cross sectional study

**[1]Dr. Vidya Ramnath Bhojane,[2]Dr. Varsha Sharad Nandedkar,[3]Dr. Priyanka Vilas Jadhav, [4]Nirmala Narayan Gaikwad**

[1]MS Ophthalmology,Associate Professor, SMBT Institute of Medical Sciences and Research Centre, Dhamangaon, Nashik, Maharashtra, India

[2]MS Ophthalmology, Professor&HOD,Govt. Medical College, Aurangabad,Maharashtra, India

[3]MBBS, Junior Resident,SMBT Institute of Medical Sciences and Research Centre, Dhamangaon, Nashik, Maharashtra, India

[4]MS OBGY, Senior Resident,PGI Nasik, Maharashtra, India

**Corresponding Author:**
Dr. Vidya Ramnath Bhojane (vidyabhojane1987@gmail.com)

**Abstract**

**Background:** Pseudoexfoliation syndrome (PXS) occurs due to the deposition of a distinctive fibrillar material in the anterior chamber of the eye. The trigger for the production of PEX material remains to be identified. Limited study has compared clinical characteristics of Pseudoexfoliation cases with non pseudoexfoliation cases.

**Methods:** This was descriptive cross-sectional study conducted in Ophthalmology department of tertiary care teaching hospital of Marathwada. Study conducted over a period of two years and 220 each pseudoexfoliation (PEX) and without pseudoexfoliation cases studied. A detailed evaluation including ophthalmic and general history, slit lamp examination, intraocular pressure measurement, gonioscopy and dilated eye examination was performed on all patients.

**Results:** Pseudoexfoliation was predominantly seen in ≥ 71 years of age (60.90%) and in males (63.18%). Hearing loss (23.18%), hypertension (21.81%), ischemic heart diseases (IHD) (16.81%) were predominant in pseudoexfoliation patients than non pseudoexfoliation patients**.**

**Conclusion:** In present study diseases like hypertension, IHD, Glaucoma and changes due to systemic diseases found to be more prevalent among Pseudoexfoliation patients.

**Keywords:** Pseudoexfoliation, Hypertension, Glaucoma, Ischemic Heart Disease, Intraocular pressure

## Introduction

Pseudoexfoliation syndrome (PEX) is an age-related systemic and generalized disorder of the extracellular matrix characterized by production of abnormal basement membrane-like material in several intraocular and extraocular tissues[1]. The multifocal production and progressive accumulation of a fibrillary extracellular material in intra- and extra ocular tissues that is either the result of an excessive production or insufficient breakdown, or both[2]. It was first described in 1917 by Lindberg[3].

It is frequently associated with open angle glaucoma, known as pseudoexfoliation glaucoma, which is the most common identifiable form of secondary open angle glaucoma worldwide[4].Despite extensive research, the exact chemical nature of the fibrillar material is unknown. It is believed to be secreted multifocally in the iris pigment epithelium, the ciliary epithelium, and the peripheral anterior lens epithelium[5]. Studies have reported that the amyloid matter of PEX is also present in heart, lungs, liver, kidney, meninges and blood vessels which may explain why patients with ocular PEX may have a history of hypertension, abdominal aorta aneurysm, angina, cardiovascular disease and stroke etc[6].

Pseudoexfoliation syndrome has been usually seen among the old age group patient[3]. The reported prevalence in different parts of the world have varied from 0% to 38% in different populations.[1] Prevalence rates increase markedly from age 50 to late 80's. The prevalence of PEX world-wide ranges from 0.5% in those aged < 60 years to 15% in those aged ≥ 60 years. The prevalence of PXF based on hospital reports from India varies between 1.87% and 13.5%[7].

The trigger for the production of PEX material yet to be identified. Very few studies have done where case of pseudoexfoliation and without pseudoexfoliation compared. With this background present study

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conducted with objectives to ascertain the association of various systemic diseases, glaucoma, hearing loss etc. with and without pseudoexfoliation.

**Material and Methods**

The present study commenced after obtaining Institutional Ethical Committee's Permission (IEC). This was descriptive cross-sectional study conducted in Ophthalmology department of tertiary care teaching hospital of Marathwada. The study was conducted over the period of two years from 20…to 20…. Minimum 189 sample size was obtained using statistical formula n = Z2(1-α/2) (1-P)/d2p[8]where P, is the prevalence of pseudoexfoliation taken as 06% from the previous study[9], Z is 1.96 at 95% confidence interval (CI), and absolute precision is 07%. Samples size was rounded to 200 but in present study total 440 participants {220 in each pseudoexfoliation (PEX) and without pseudoexfoliation (Non PEX) group} were included after explaining the procedure and purpose of the study and obtaining informed consent. Patients who are 50 and above years of age, either gender residing within the catchment area of the tertiary care hospital were included and those who are not willing to participate, having traumatic cataract, uveitis were excluded.

Validation, practicality and applicability of questionnaire was assessed by pilot study. It was carried out using predesigned questionnaire among 10 individuals. According to answers obtained and difficulties faced during pilot study, rectification was done and questionnaire modified accordingly. Detailed ophthalmic history viz. complaints of diminish vision-its onset, duration and progress, redness, pain, watering of eyes, discharge from eyes, photophobia, hearing loss, family history and past history mainly about sensorineural hearing loss, hypertension, diabetes mellitus and ischemic heart disease, drug history etc. were obtained from every selected patient.

The WHO recommended[10] sitting position and technique was used for measurement of blood pressure. The hypertensive status defined according Joint National Committee (JNC7)[11] criteria and those individuals currently taking antihypertensive treatment. Arterial hypertension was diagnosed if average of two successive reading of systolic and diastolic blood pressure ≥ 140 and ≥ 90 respectively. Based on medical record and/or ischemic changes on electrogram (ECG) patients considered as known case of ischemic heart disease. Diabetes status was defined if the patient is a known case, taking oral hypoglycemic drugs and for suspected cases BSL fasting and post prandial was done. Consultation of General Medicine department was done for the diagnosis of systemic diseases. Hearing loss was assessed on audiogram by ENT specialist.

Diagnosis of PEX was made by slit-lamp examination after diagnostic mydriasis with 01 drop of 0.5% tropicamide. The criterion used to diagnose PXS was the presence of pseudoexfoliation material on one or more anterior segment structures. Since the presence of pseudo exfoliative material on lens is the most consistent and prominent feature of PEX, so to prevent under estimation of the prevalence, all subjects who were psuedophakic or aphakic in any eye were excluded from the study the participants were classified as having PEX if any pseudoexfoliation material was present in at least one eye.

Gonioscopy examination was done with the help of Goldman four mirror gonioscope, in a dark room and with use of short, narrow slit-beam to avoid constricting of pupil and artificially opening the angle. Cornea was anaesthetized by instilling 0.5% proparacaine eye drops in conjunctival sac. The angle of anterior chamber was examined. A thorough examination including visual acuity, anterior segment and posterior segment examination, measurement of intraocular tension and, electrocardiogram, biochemical blood analysis, audiometry, and blood pressure examination was done for every patient.

**Statistical Analysis**

The questionnaires were checked for completeness, and the data entered in MS excel and Statistical Package for Social Sciences (SPSS version 21.0) software was used for descriptive and inferential analysis. Chi-square test, Fisher's exact test was used to check statistical association. Level of significance at 5% ($P < 0.05$) was considered statistically significant (two-tailed)

**Results**

In present study 440 patient were included, 220 (50%) were with pseudoexfoliation (PEX) and 220 were without pseudoexfoliation (50%) (Non PEX).Age and Gender distribution of patients shown in Table no 01. Statistically no difference was observed in between age, gender and patients' groups.

**Table 1:** Age and Gender distribution of the participants (n=440)

| Age Groups (Years) | Patients Groups | | Frequency (%) |
|---|---|---|---|
| | PEX (%) | Non PEX (%) | |
| 50-60 Yrs. | 36 (16.36%) | 41 (18.63%) | 77 (17.26%) |
| 61-70 Yrs. | 50 (22.72%) | 48 (21.81%) | 98 (22.27%) |
| ≥ 71 Yrs. | 134 (60.90%) | 131 (59.54%) | 265 (60.22%) |
| Total | 220 (50%) | 220 (50%) | 440 (100%) |
| Chi-Square ( 2) 3.99 d.f:02 P:0.81 non-Significant | | | |
| **Gender** | **PEX (%)** | **Non PEX (%)** | **Frequency (%)** |

ISSN: 0975-3583, 0976-2833 VOL13, ISSUE01, 2022

| | | | |
|---|---|---|---|
| Male | 139 (63.18%) | 142 (64.54%) | 281 (63.86%) |
| Female | 81 (36.81%) | 78 (35.45%) | 159 (36.13%) |
| Total | 220 (50%) | 220 (50%) | 440 (100%) |
| Fisher's Exact Test: P:0.84 non-Significant | | | |

Inpseudoexfoliation (PEX) 23.18% patients had hearing loss while it was just 10% in non pseudoexfoliation (Non PEX). Hearing loss found to be more in pseudoexfoliation patients (23.18%) and difference was found to be statistically significant. Glaucoma found in 15.45% (34) pseudoexfoliation patients while it was seen in 11.81% (26) of non pseudoexfoliation cases and association found to be statistically non-significant (Table no 02).

**Table 2:** Distribution of hearing loss & Glaucoma among patients (n=440)

| **Hearing Loss** | **Patients Groups** | | **Frequency (%)** | **Fishers Exact Test** |
|---|---|---|---|---|
| | **PEX (%)** | **Non PEX (%)** | | |
| Present | 51 (23.18%) | 22 (10%) | 73 (16.59%) | P: 0.0003 Significant |
| Absent | 169 (76.81%) | 198 (90%) | 367 (83.40$%) | |
| Total | **220 (50%)** | **220 (50%)** | 440 (100%) | |
| | **Patients Groups** | | Frequency (%) | Fishers Exact Test |
| Glaucoma | **PEX (%)** | **Non PEX (%)** | | |
| Present | 34 (15.45%) | 26 (11.81%) | 60 (13.63%) | P: 0.33 Non-Significant |
| Absent | 186 (84.54%) | 194 (88.18%) | 380 (86.36%) | |
| Total | 220 (50%) | 220 (505) | 440 (100%) | |

Regarding systemic disease out of 440 patients 76 (17.27%) were cases of hypertension. Out of that 60 (78.94%) were know case of hypertension and 16 (21.05%) were newly diagnosed. Diabetes was seen in 39 (8.86%) patients out that 29 (74.35%) and 10 (25.64%) were know and newly diagnosed cases of diabetes respectively. In present study ischemic heart disease was seen 57 (12.95%) patients, in which 77.19% (44) were known cases while 22.80% (13) were newly diagnosed.Hypertension and Ischemic diseases found to be more in pseudoexfoliation (PEX) patients than without pseudoexfoliation (non PEX) while diabetes seen in more in non pseudoexfoliation (PEX) group. Distribution of systemic diseases and their statistically association shown in table no 03.

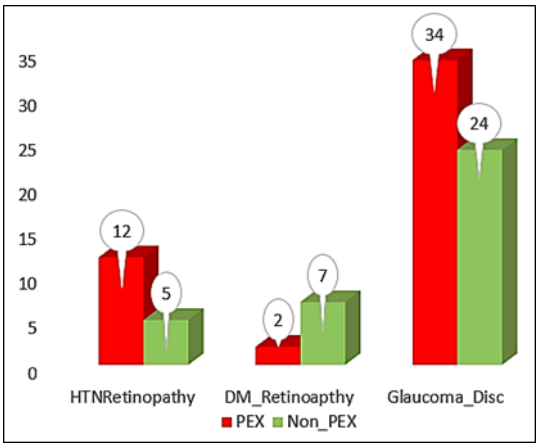
**Table 3:** Distribution of systemic diseases among the participants (n=440)

| **Systemic diseases** | **Patients Groups** | | **Frequency (%)** |
|---|---|---|---|
| | **PEX (%)** | **Non PEX (%)** | |
| HTN Present | 48 (21.81%) | 28 (12.72%) | 76 (17.27%) |
| HTN Absent | 172 (78.18%) | 192 (87.27%) | 364 (82.72%) |
| Fisher's Exact Test: P:0.016 Significant | | | |
| DM Present | 14 (06.36%) | 25 (11.36%) | 39 (08.86%) |
| DM Absent | 206 (93.63%) | 195 (88.63%) | 401 (91.13%) |
| Fisher's Exact Test: P:0.09 non-Significant | | | |
| IHD Present | 37 (16.81%) | 20 (09.09%) | 57 (12.95%) |
| IHD Absent | 183 (83.18%) | 200 (90.90%) | 383 (87.04%) |
| Total | 220 (50%) | 220 (50%) | 440 (100%) |
| Fisher's Exact Test: P:0.02 Significant | | | |

*HTN: Hypertension, DM: Diabetes Mellitus, IHD: Ischemic Heart Disease

Regarding hypertensive and diabetic fundus changes, out of 48 hypertensives pseudoexfoliation patient's hypertensive retinopathy seen in 12 (25%) patients whereas out of 28 non pseudoexfoliation hypertensive patients 05 (17.85%) had similar changes while out of 14 diabetic pseudoexfoliation patients and 25 diabetics non pseudoexfoliation patients 02 (14.28%) and 07 (28%) patients showed diabetic retinopathy respectively. All most all glaucoma patients (34, 100% and 24, 92%) of both groups showed glaucomatous disc changes on fundus examination. (Graph 01)

ISSN: 0975-3583, 0976-2833 VOL13, ISSUE01, 2022




**Graph 1:** Fundus Changes in PEX and non-PEX patients

Gonioscopy was done using Goldmann 3 mirror lens. Non statistical association was found in between gonioscope grades and type of patients (table no 04). In present study 28.18% (62) pseudoexfoliation cases and 71.81% (158) cases were unilateral and bilateral respectively.

**Table 4:** Distribution of Gonioscope grades of the participants (n=440)

| Gonioscope grades | Patients Groups | | Frequency (%) |
|---|---|---|---|
| | PEX (%) | Non PEX (%) | |
| + 1 | 00 (0.00%) | 00 (0.00%) | 00 (0.00%) |
| + 2 | 07 (3.18%) | 06 (2.72%) | 13 (02.95%) |
| + 3 | 26 (11.81%) | 30 (13.63%) | 56 (12.72%) |
| + 4 | 187 (85.00%) | 184 (83.63%) | 371 (84.31%) |
| Total | 220 (50%) | 220 (50%) | 440 (100%) |

Chi-Square Test ( 2): 0.38, df:02 P:0.82non-significant

Anterior segment slit lamp examination of pseudoexfoliation deposit of patient shown in table no 05 and difference found to be non-significant. In present study peri-pupillary iris atrophy seen in 34 cases, small depth anterior chamber seen in 07 patients and in 05 and 04 cases had pigment on lens and cornea respectively.

**Table 5:** Distribution of pseudoexfoliation deposit

| Clock hours | On Lens Anterior capsule | On Pupillary margin of Iris | Frequency (%) |
|---|---|---|---|
| < 6 | 40 (37.03%) | 33 (29.46%) | 73 (33.18%) |
| > 6 | 68 (62.96%) | 79 (70.53%) | 147 (66.81%) |
| Total | 108 (49.09%) | 112 (50.90%) | 220 (100%) |

Fisher's Exact Test: P:0.25 non-Significant

**Discussion**

In present cross sectional study total 440 patient were studied over period of two years. In each group 220 patients were included. Pseudoexfoliation was predominantly seen in ≥ 71 years of age (60.90%) and in males (63.18%) but age groups and gender found to be non-significantly associated with pseudoexfoliation (Table 01).Rao R.Q. *et al.*[3] reported prevalence of PEX 02.6% in patients less than 70 years of age, which increased to 13.04% in patients 70 years and above elder. In a study by Andrikopoulos GK *et al.* [12] in Greek population, reported increase in prevalence of PEX from 1.2% in the 06th decade to about 34% in older than 80 years. This study reported higher prevalence of PEX in older. A population-based study in the United States found a prevalence of PEX 0.67% in people aged 52-64 years, 02.6% in people aged 65-74 years, and 05% in people aged 78-85 years[13]. Arvind H *et al.* [5] too reported a significant increase in prevalence of pseudoexfoliation with age but no sex predilection found in his study.

Hearing loss was predominant in pseudoexfoliation patients compared to non pseudoexfoliation patients. In PEX 23.18% patients had hearing loss while it was just 10% in Non PEX (table 02). Hearing loss found to be statistically associated with patients' group.Zojaji R*et al.*[14] conducted matched case control study on 33 cases and controls. He reported 49 out of 66 ears (75.2%) in the PXS group and 27 ears (40.9%) in the control group had sensory neural hearing loss (SNHL) and the difference found to be statistically significant.

In our study glaucoma found in 15.45% (34) pseudoexfoliation patients while it was seen 11.81% (26) non pseudoexfoliation cases and this association found to be statistically significant (Table 02) Arvind H *et al.* [5] reported high intraocular pressure (>21 mm Hg) in 18 cases (16.7%) of PEX, while 16 (14.8%)

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had occludable angels and 14 cases (13%) had PEX glaucoma. Astalos JP *et al*.[15] reported 03.6% the prevalence of pseudoexfoliation syndrome and 09.4% prevalence of primary open angle glaucoma, out of which 23.6% were the cases of pseudoexfoliation glaucoma. In Rao RQ *et al*. [3]study 40% (48) PEX patients had high intraocular pressure.

Systemic diseases like hypertension and ischemic heart diseases were prevalent in PEX. Out of 220 PEX patients almost twenty-two percent participants and 13% patients out of 220 non PEX had high blood pressure in present study and this difference found to be statistically significant. (Table 03). Rao RQ *et al*.[3] reported 16.8% PEX case were the hypertensive.In present study number of diabetes cases found to be low in pseudoexfoliation group (06%) than non pseudoexfoliation group (9%) and non-statistically significant association observed. (Table 03) Rao RQ *et al*.[3] reported 10.8% prevalence of diabetes among PEX patients in his study.Ischemic heart diseases (IHD) in PEX and non PEX group were 16.81% and 09.09% respectively and IHD found to be statistically associated. (Table 03) Joshi A K *et al.* [16] conducted study on patients with pseudoexfoliation syndrome undergoing manual small incision cataract surgery in a teaching hospital. He too reported that diseases such as hypertension, diabetes mellitus, ischemic heart disease (IHD), Parkinsonism were systemic diseases associated with pseudoexfoliation patients.

Regarding hypertensive and diabetic fundus changes, out of 48 hypertensives pseudoexfoliation patient's hypertensive retinopathy seen in 12 (25%) patients whereas out of 28 non pseudoexfoliation hypertensive patients 05 (17.85%) had similar changes while out of 14 diabetic pseudoexfoliation patients and 25 diabetics non pseudoexfoliation patients 02 (14.28%) and 07 (28%) patients showed diabetic retinopathy respectively. All most all glaucoma patients (34, 100% and 24, 92%) of both groups showed glaucomatous disc changes on fundus examination. (Graph 01)

In present study non statistical association was found between gonioscope grades and type of patients (table no 04). In present study 28.18% (62) and 71.81% (158) pseudoexfoliation cases were unilateral and bilateral respectively. Arvind H *et al*. [5] reported PEX unilateral in 53 cases (49.1%) and bilateral in 55 cases (50.9%) Triveni C *et al*. [17] in her study reported that 31 (27.7%) eyes had a gonioscopy PXF angle, 71 (63.4%) eyes had gonioscopy pigments, 49 (43.80%) eyes had gonioscopy sampaolesi's line while 67 (59.82%), 31 (27.68%), 9 (8.04%) and 5 (4.46%) had gonioscopy Shaffer's grade IV, III, II and I respectively. Somewhat similar distribution of pseudoexfoliation material found on anterior capsule of lens and pupillary margin of iris (table 05).

**Conclusion**

Pseudoexfoliation syndrome is the age-related systemic disorder with characteristic eye manifestations. In present study systemic diseases like heating loss, hypertension and IHD found to be more prevalent among PEX. Other illness like diabetes and glaucoma found to be more predominant in PEX than non PEX but the difference wasn't statistically significant. Glaucoma and changes due to systemic diseases found to be more prevalent in pseudoexfoliation patients. Further study will be required for better understanding of this senile disorder.

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