

Prevalence and Ocular Manifestations of Pseudoexfoliation Syndrome Among Patients Scheduled for Cataract Surgery in a Teaching Hospital in North India

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ABSTRACT

Introduction: The correct diagnosis of PXF is highly examiner-dependent. PXF syndrome often remains undiagnosed especially because of missing the early subtle signs. To study the prevalence and ocular manifestations of Pseudoexfoliation syndrome (PXF) among patients scheduled for cataract surgery in a teaching hospital in the north Indian state of Himachal Pradesh.

Material and methods: In this cross-sectional study, patients with cataract scheduled for Manual small incision cataract surgery (MSICS) from September 2017 to March 2019 were screened for the presence of PXF. A thorough pre-operative evaluation was performed including slit lamp examination, gonioscopy, tonometry and funduscopy. Clinical and demographic profile of patients with PXF and the intra-ocular manifestations were recorded.

Results: A total of 280 patients were evaluated. Of these, 64 patients (22.9%) had PXF syndrome. Thirty-seven patients (57.8%) were males and 27 (42.2%) were females. The mean age was 68 years (range 51-84 years) and majority (42.2%) was in the age group of 61 to 70 years. PXF prevalence was seen to be maximum in the age group 81 years and above (26.3%) and least in the 51 to 60 years group (16.9%). Morphologically, nuclear cataract was the most common type of cataract observed (26.6%) followed by cortical cataract with nuclear sclerosis (18.8%). PXF was seen in both eyes in 68% of patients, while unilateral involvement was seen in 32%. Mean pupillary dilation was 5.92 (± 1.25) mm, which was significantly lower than the non-PXF cohort (7.14 ± 0.35 mm, $P=0.000$).

Conclusion: There is relatively higher prevalence of PXF in Himachal Pradesh. Hence, it is important to diagnose the ocular manifestations of PXF syndrome in all patients, especially those posted for cataract surgery to ensure minimal complications and to achieve good post-operative visual outcome.

Key words: Cataract, Manual Small Incision Cataract Surgery, Prevalence, Pseudoexfoliation, Pseudoexfoliation in North India

INTRODUCTION

Pseudoexfoliation (PXF) syndrome is a systemic disorder first mentioned in 1917 by Lindberg, a Finnish ophthalmologist and further described in 1923 by Alfred Vogt.¹ PXF is observed as grayish-white fibrillogranular material on pupillary margin, anterior lens capsule, iris, ciliary body, corneal endothelium, trabecular meshwork, anterior hyaloid surface, intraocular lens and posterior lens capsule.² The

epithelial cells of the basement membrane of ciliary body, iris and lens epithelium produce the fibrillogranular material. On histopathology, the deposits are composed of fibrillin, an elastin forming the elastic fibers and fibrils, which are non-collagenous basement membrane material. Laminin, glycosaminoglycans and hyaluronic acid coat the fibers and fibrils.³

The correct diagnosis of PXF is highly examiner-dependent. PXF syndrome often remains undiagnosed especially because of missing the early subtle signs. The importance of diagnosing PXF on routine ocular examination lies in the fact that it is associated with increased risk of complications during cataract surgery primarily due to two pathological manifestations, which are zonular weakness and poor dilatation of pupils. Such patients can have as high as five-times greater risk of intra-operative complications including posterior capsular rupture, vitreous loss, zonular dialysis, secondary cataract, capsular phimosis and corneal decompensation.⁴ PXF is commonly seen in the elderly and is often accompanied by open and closed-angle glaucoma.²

The prevalence of PXF shows wide variation worldwide because of various factors like age, ethnic predisposition, geographical location, environmental factors, etc. Worldwide, higher prevalence rates of PXF syndrome have been found in Northern European, Scandinavian and Mediterranean region.⁵

Single nucleotide polymorphisms (SNPs) in Lysyl Oxidase-Like 1 (LOXL1) gene have been associated with PXF.⁶⁻⁸ Ethnicity-based differences in the association of LOXL1 polymorphisms with PXF have also been shown. A study from Chandigarh in North India showed lack of association

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between LOXL 1 SNP and PXF in “north Indian” population but the study didn’t categorize the population into various ethnic groups considering the setting of the study being a tertiary care centre with heterogeneous population reporting to the OPD.⁹ Ethnic diversity in north India is well known.¹⁰ A study from extreme north India showed higher prevalence of 26.32% in patients scheduled for cataract surgery in camp patients in the Kashmir region.¹¹ Since the geographic location and environmental factors predispose to PXF, it was important to find out prevalence rates in our state because such significant prevalence rates warrant detailed slit lamp examination so that surgeons are better prepared to avoid any intra-operative complication and plan appropriate intra-operative and post-operative intervention in PXF eyes for better postoperative outcome.

MATERIAL AND METHODS

This was a cross-sectional study carried out in the ophthalmology department of a teaching hospital in the north Indian state of Himachal Pradesh. Patients who presented to the OPD with significant cataract and scheduled for manual small incision cataract surgery between September 2017 and March 2019 were included. The study was approved by the Institutional Ethics Committee and adhered to the tenets of the declaration of Helsinki. Written and informed consent was taken from all patients. Patients <50 years old, those with traumatic or complicated cataract, and history of previous ocular surgery were excluded.

Detailed history was recorded and best-corrected visual acuity (BCVA) was measured using Snellen's chart. IOP was measured by non-contact tonometer. Slit lamp examination was performed for anterior segment evaluation and PXF deposits were noted on the pupillary margin, iris, anterior lens capsule and cornea before and after pupil dilation with 5% Phenylephrine + 0.8% Tropicamide. Cataract was graded according to Lens Opacities Classification System 3 (LOCS 3). Patients were operated by two surgeons with more than 15 years experience in MSCIS.

STATISTICAL ANALYSES

Descriptive statistics were used to analyze the prevalence, demographic and clinical characteristics as well as the intra-ocular manifestations. Independent T-test was used to compare the mean pupillary dilation between the PXF and non-PXF cohort, as well as between eyes with PXF deposition on lens, pupillary margin or iris alone and those with PXF material on all three ocular structures combined. A *P*-value of ≤ 0.05 was considered as statistically significant. All statistical analyses were performed using the Statistical Package of Social Sciences (SPSS) v23.

RESULTS

Of the 280 patients screened, 64 were diagnosed with Pseudoexfoliation syndrome (prevalence of 22.9%). The patients were residents of districts Solan, Sirmour, Kinnaur and Shimla situated in northwestern Himalayas. Thirty-seven patients (57.8%) were males and 27 (42.2%) were females.

Age (Years)	Sex		Number of patients with Pseudoexfoliation (%)
	Males	Females	
51-60	6	6	12 (18.8%)
61-70	15	12	27 (42.2%)
71-80	16	4	20 (31.3%)
81 and above	0	5	5 (7.8%)
Total	37	27	64

Table-1: Age and sex distribution of patients with Pseudoexfoliation

Age (Years)	Number of patients with PXF	Total number of patients	Percentage of patients with PXF
51-60	12	71	16.9%
61-70	27	111	24.3%
71-80	20	79	25.3%
81 and above	5	19	26.3%
Total	64	280	22.9%

Table-2: Age group wise distribution of PXF patients to total number of patients

PXF material	Number of operated eyes (%)
Pupillary Margin	18 (28.1%)
Iris	6 (9.4%)
Lens	19 (29.7%)
Iris, Pupillary margin and lens	14 (21.9%)
Pupillary margin and Lens	7 (10.9%)

Table-3: Distribution of PXF in ocular structures

Pupillary Dilation	Number of operated eyes with PXF (%)
<5mm (poor)	6 (9.4%)
5-7mm (fair)	46 (71.8%)
>7mm (good)	12 (18.8%)

Table-4: Maximum Pupillary Dilation observed

Type of cataract	Number of operated eyes with PXF (%)
Hyperature	6 (9.4%)
Mature	11 (17.2%)
Cortical	6 (9.4%)
Nuclear Cataract	17 (26.6%)
Cortical & nuclear	12 (18.8%)
Posterior subcapsular	8 (12.5%)
Posterior subcapsular & nuclear	4 (6.3%)
Total	64

Table-5: Distribution of morphological type of cataract with PXF

The mean age was 68 years (range 51-84 years) and majority (42.2%) was in the age group of 61 to 70 years. Age and sex-wise distribution has been depicted in table 1.

The number of patients in the age group of 81 years and above had the highest prevalence of PXF syndrome (26.3%),

IOP (mm of Hg)	Number of operated eyes with PXF (%)
≤10	5 (7.8%)
11-15	26 (40.6%)
16-20	23 (36.0%)
21 & above	10 (15.6%)

Table-6: Pre-operative intraocular pressure (IOP)

Best-corrected visual acuity	Number of operated eyes with PXF (%)
6/6- 6/9	0
6/12- 6/18	1 (1.6%)
6-24- 6/36	12 (18.8%)
6/60 & less	51 (79.7%)

Table 7: Pre-operative best-corrected visual acuity

followed by 71-80 years group (25.3%). Age-group wise distribution of patients with PXF to total number of patients screened is shown in table 2.

Majority of the patients (47%) had agriculture as their mode of income followed by those working in the public works department or construction activities (9.4%).

PXF was seen in both eyes in 34 (68.0%) patients, while 16 (32.0%) had unilateral involvement. 14 patients had pseudophakia and hence laterality was not commented.

All clinical and intra-ocular characteristics have been described for the operated eye in all patients with PXF. PXF material was present on the lens in 19 (29.7%) cases and on the pupillary margin in 18 (28.1%) cases. Fourteen patients (21.9%) had PXF material on the lens, iris and the pupillary margin together. PXF material was present on the iris in 6 (9.4%) cases and lens and pupillary margin were involved together in 7 (10.9%) patients while in 3 (4.7%) cases, PXF deposits were seen on the endothelial surface of cornea (Table 3).

Poor pupillary dilation (<5mm) was observed in 6 cases (9.4%). Pupillary dilation was fair in 71.8% cases (n=46) and 18.8% cases (n=12) had good dilation. Mean pupillary dilation was 5.92 (±1.25) mm, which was significantly lower than the non-PXF cohort (7.14±0.35 mm, $P=0.000$). Mean pupillary dilation in patients with PXF material distributed on the pupillary margin, iris and lens together was 5 (±0.66) mm, whereas in patients with PXF material on lens and pupillary margin alone it was 6.32 (±1.2) mm and 5.83 (±1.2) mm, respectively. Patients with PXF material on the pupillary margin, lens and iris together had significantly lower pupillary dilation than those with PXF material on the lens alone ($P=0.014$). In patients with PXF alone on the iris, mean pupillary dilation was 7mm (Table 4).

Morphologically, nuclear cataract was the most common type of cataract observed (26.6%), followed by cortical cataract with nuclear sclerosis (18.8%). Distribution of morphological type of cataract is depicted in table 5.

The increased intraocular pressure was noticed in 10 eyes (15.6%) in our study. The mean intraocular pressure was 16.3 mm of Hg. Two patients each (3.2%) had open-angle glaucoma and lens-induced glaucoma (Table 6).

Pre-operative best-corrected visual acuity was recorded. Around 80% patients had visual acuity < 6/60. In 19 % cases, it was between 6/36 and 6/24 (Table 7). Five patients in our analysis exhibited hypertension, 3 patients had diabetes mellitus and hypertension together. Two patients had hypertension with ventricular ectopics and 1 patient each had paroxysmal ventricular tachycardia, coronary artery disease, severe xerosis of skin, pyocoele of chest and chronic obstructive pulmonary disease.

DISCUSSION

In this study, we observed a high prevalence of PXF syndrome among patients with cataract planned for MSICS. These prevalence rates are higher than those reported from south India (22.1%) and lower than the rates from the north Indian Kashmir region (26.3%).¹¹⁻¹³

The prevalence of PXF syndrome is found to be more in the Scandinavian & northern European region. Various studies report a high prevalence of PXF ranging from 23% in Sweden¹⁴, 30% in Iceland¹⁵ and 31% in Finland.¹⁶ In southwestern Greece, in a cross-sectional study of patients admitted at the hospital for cataract surgery the prevalence of PXF syndrome was reported as 27.9%.¹⁷ Lee et al. from Singapore found the PXF prevalence to be highest amongst the Indians than Malays and Chinese groups.¹⁸ The reported prevalence rates of PXF syndrome in patients scheduled for cataract surgery shows extensive variations with Ethiopia (39.3%), Finland (30.8%), Greece (28%), Portugal (25.3%) and Egypt (4.1%) (7, 19-21).

In a hospital-based study from South India, the prevalence of PXF syndrome in patients scheduled for cataract surgery was 22.1% with a maximum prevalence of 35.8% in the age group of 81 years and above.¹³ Another population-based study from rural south India reported the prevalence rates of PXF as low as 3.8%.¹² From the northwestern Himalayan region, limited data is available and very few studies on the prevalence of PXF syndrome in patients with cataract have been conducted. Sufi et al from the neighboring region of Kashmir reported a high prevalence rate of 26.32% among patients scheduled for cataract surgery in a camp-based study, which is higher than that reported in our study. The authors attributed association of PXF with outdoor activity, environmental factors (solar radiation, UV exposure), ethnic origin and genetic factors.¹¹ Moreover, this was a camp-based study in contrast to ours that was a hospital-based cross-sectional analysis, which could partly explain the relatively higher rates of PXF prevalence reported by the authors despite of the geographical and environmental similarities. Geographical and environmental factors play an important role in PXF prevalence. The prevalence of PXF is known to increase with latitude shift away from the Equator.²² Another important factor that affects the prevalence of PXF is solar radiation exposure.²³ Solar radiation increases in intensity as altitude increases. Outdoor activity also independently increases the solar exposure and this UV radiation can upregulate the exfoliative material. Cold weather can increase the precipitation of PXF on the structures surrounding the

anterior chamber.²⁴

All these factors are prevalent in our study population, which probably reflects on the higher prevalence of PXF. Himachal Pradesh state is a North-western Himalayan state between with extreme cold during winters and altitude as high as 6500+ meters above sea level. Our area is at an altitude of 1600-2200 meters above sea level. Most people have increased outdoor activity, as the predominant profession is agriculture. Sun gazing due to extremely cold weather also adds up to the solar radiation exposure.

Pseudoexfoliation syndrome predominantly affects the elderly age group and cataract in majority of patients is also age-related. The association of PXF with ageing and blindness has public health implications for India, especially considering the burden of cataract as well as increased rate of complications of cataract surgery in patients with PXF syndrome. There is association between PXF and cataracts, possibly due to ocular ischemia and defective antioxidant mechanism. Moreover, cataracts appear sooner and progress quicker in these patients.

The prevalence of PXF increased with increasing age in our study population, which is in line with that reported in other studies. In a hospital-based study by Govetto et al., PXF syndrome was not reported in patients below 50 years posted for cataract surgery. Two patients (6.1%) between 50-60 years, 11 (7.3%) patients between 60-70 years, 83 (19.1%) between 71-80 years and 149 (31.7%) above 80 years had PXF syndrome.²⁵ Similar observations were noted by Al-Shaer et al in Yemen, wherein 10.1% patients between 41 and 50 years old and 28.8% were >81 years old had the syndrome.²⁶

In 2003, Arvind H et al studied the profile of PXF in a population-based study in rural south India. They observed significant increase in prevalence with age but no sex predilection. There was a significantly higher prevalence of cataract among people with PXF compared to those without PXF ($p=0.014$). Raised IOP was seen in 16.7% of people with PXF.¹² We observed a male preponderance in our study population with PXF. This distribution is consistent with the observation of Pranathi et al. who, in their study of 52 patients observed 53.8% males and 46.2% females.²⁷ Lamba et al also reported a higher prevalence of PXF among males.²⁸ However, the Reykavik Eye Study has suggested female predominance among patients with PXF.²⁹

More than 65% of the patients in our study had bilateral involvement. Most studies have reported a predominantly bilateral involvement with PXF, as the unilateral disease more commonly progresses to a bilateral condition. In PXF, there is an initial unilateral involvement in 40 to 50% of patients that becomes bilateral within 5 years. Gelaw and Tibebe reported bilateral involvement in 66.7% patients in their study.³⁰

The intra-ocular distribution of PXF material in our study population is consistent with that reported previously. Lens was the most commonly affected (29.7%) followed by the pupillary margin (28.1%) and the pupil, iris and lens together (21.9%). In a study by Idakwo et al, all patients had PXF

material on the peripheral zones of the lens and the pupillary margin.³¹ Joshi RS et al. reported the distribution of PXF material on the iris, pupil, and lens in 30.9% of the cases in their study.¹³

The mean pupillary dilation was significantly lower than in patients who did not have PXF, especially in patients PXF material in the pupillary margin, lens and iris together. In a study by Philip et al., 96.7% eyes diagnosed with PXF syndrome had pupillary dilation of <6mm.³² Govetto et al. reported that pupillary dilation is significantly less in PXF patients than in non-PXF patients.²⁵

Morphologically, nuclear cataract was the most common type of cataract observed (26.6%) followed by cortical cataract with nuclear sclerosis (18.8%). These findings are similar to previously reported studies. However, Joshi RS et al., in their study noticed 43.4% cases with hypermature cataract, which could be due to the belief in rural India that cataract surgery is required after it matures.¹³

Numerous studies have shown a correlation between increased IOP and PXF syndrome. Increased intraocular pressure was noticed in 15.6% patients in our study. The mean intraocular pressure was 16.3 mm of Hg. Two patients each (3.2%) had open angle glaucoma and lens-induced glaucoma. Low incidence of glaucoma in our study could be an incidental finding in PXF syndrome, as suggested by Philip et al.³² Lamba and Giridhar (9%), a North Nigerian study (4.4%) and the Andhra Pradesh study (4.2%) have reported low prevalence of glaucoma.^{12,28,31} In a study by Joshi RS et al., increased IOP was observed in 9.3% eyes. The mean IOP was 24 (± 6) mm. 8% eyes had open-angle glaucoma, 0.4% eyes had chronic angle-closure glaucoma and 0.9% eyes had lens-induced glaucoma.¹³ We also observed systemic conditions such as hypertension, diabetes, coronary artery disease and ventricular ectopics in our study cohort. Mitchell et al. correlated PXF with increased vascular risk in the Blue Mountain study.³³

The association of PXF syndrome in patients of cataract can have an impact on surgical outcome. Therefore, it is of utmost importance to diagnose PXF in all patients especially those presenting with cataract so as to avoid complications and improve surgical outcome. There is lack of published data on PXF prevalence rates in North India. This study was conducted to analyze the prevalence of PXF syndrome in this north Indian state as majority of the risk factors proposed to be involved in the etiology of PXF syndrome are widespread in this region.

CONCLUSION

The prevalence of PXF in Himachal Pradesh is higher than other parts of the Indian sub-continent. It is important to be vigilant about PXF syndrome as a pre-operative diagnosis helps in avoiding various intraoperative complications, thus resulting in better surgical outcome in predisposed populations like that of our region.

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