PROPORTION AND CLINICAL PROFILE OF PSEUDOEXFOLIATION SYNDROME IN CATARACT PATIENTS

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ABSTRACT
Background: Pseudoexfoliation (PXF) syndrome is a systemic condition characterised by deposition of fibrillar material in the anterior chamber of the eye. PXF is associated with glaucoma and complications during cataract surgery. Study aims to estimate the proportion of pseudoexfoliation syndrome among cataract patients undergoing small incision cataract surgery and to find the clinical profile of pseudoexfoliation syndrome. Materials and methods: A prospective study including 300 cataract patients posted for small incision cataract surgery was done in a tertiary care centre. History, pupillary light reflex, intraocular pressure, central corneal thickness and endothelial cell count were noted and slit lamp examination for distribution of exfoliative material done. Pupils dilated and dilation measured, lens nucleus graded and fundus examination for cup disc ratio done. Data collected and entered in Microsoft Excel and analysed using SPSS version 16. Proportion of PXF calculated and other variables studied using chi square test for qualitative and t test for quantitative variables. Results: Among the 300 cataract patients studied the proportion of PXF was 18% (54eyes). Significantly high proportion of eyes with PXF had mature cataract, grade IV nuclear sclerosis, subluxated lens, low endothelial count and Central Corneal Thickness, poor pupillary dilation, high intra ocular pressure and Cup disc ratio. Conclusion: Among cataract patients 18% eyes have pseudoexfoliation which is associated with features rendering cataract surgery difficult. Hence a thorough awareness of PXF, proper slit lamp examination is mandatory to minimize complications during surgery.

KEYWORDS: Pseudoexfoliation, cataract, clinical profile.

INTRODUCTION
Pseudoexfoliation (PXF) is accumulation of grey white fibrogranular extracellular material produced by abnormal basement membranes of ageing epithelial cells in anterior segment of eye.[1] It can be identified under slit lamp examination, but is sometimes overlooked.

Pseudoexfoliation is frequently associated with open angle glaucoma, poor pupillary dilation, poor zonular integrity and low endothelial count which can render cataract surgery difficult.[2] This study aims to estimate the proportion of pseudoexfoliation syndrome among cataract patients undergoing small incision cataract surgery in a tertiary care centre and to find the clinical profile of pseudoexfoliation syndrome in comparison to those without the syndrome.

MATERIALS AND METHODS
This was a prospective study done in the Department of Ophthalmology in a tertiary care centre from July 2016 to July 2017. The study was approved by the review board of the institution. All patients with senile or presenile cataract admitted for small incision cataract surgery were included. Patients with congenital, developmental, metabolic or traumatic cataract, ocular inflammatory conditions like uveitis and those with preexisting retinal or optic nerve diseases were excluded.

Written informed consent from all the patients included in the study was taken after fully explaining the procedure and purpose of study. A detailed history according to the proforma prepared was taken (includes name, age, sex, place and phone number, comorbidities like diabetes, hypertension and coronary artery disease). Torch light used for assessing pupil size and briskness of direct pupillary light reflex. Slit lamp examination was done to note the distribution of exfoliative material, iris characteristics like iris atrophy and pigmentation of iris, and phacodonesis. Intraocular pressure was measured using non contact tonometer. Central corneal thickness and endothelial cell count was measured using SP 3000P Topcon specular microscope with pachymeter. Pupils
were dilated using 0.8% Tropicamide and 5% Phenylephrine combination topical eyedrops instilled 3 times 20 min apart and pupil dilation measured using callipers and lens nucleus was graded based on colour of nucleus as:

a) Green: GrI 
b) Yellow: GrII 
c) Amber: GrIII 
d) Red: GrIV.

Stage of cortical cataract as whether immature, mature or hypermature was also noted. Slit lamp biomicroscopy with 90 Dioptre lens was done to study size of optic disc and cup disc ratio.

Data was collected and entered in Microsoft Excel and statistical analysis, done using SPSS 16. Proportion of PXF and each clinical features were calculated. Variables were studied using chi square test for qualitative and t test for quantitative variables. Mean of few quantitative variables were also calculated.

RESULTS
1) Proportion of PXF
Out of the 300 eyes posted for cataract surgery in the Department of Ophthalmology, in our institution 54 (18%) had PXF and 246 eyes (82%) had no PXF.

2) PXF versus Age
The mean age of the two group (with and without PXF) were comparable (66 and 64 years). The age group of patients with PXF ranged from 53 to 82 years. (Fig 1).

A significant relation could not be made between age and PXF, but this study showed that prevalence of PXF increased with age. When 37% of eyes with PXF was in the age group 71-80 years, eyes without PXF was only 23.9%.

3) Gender in PXF
This study showed no significant relation between PXF and sex. But the male to female ratio was higher with PXF (28:26 ie; 1.07:1) as compared to patients without PXF (113:133 ie; 0.84:1).

4) Distribution pattern of PXF
Among patients with PXF 49 (90.74%) had the deposits over anterior lens capsule of which 14 (29.6%) had deposits over anterior surface of lens alone and the rest had deposits over multiple sites. (Table 1).

Table 1: Distribution pattern of pseudoexfoliation deposits.

<table>
<thead>
<tr>
<th>Site of PXF</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior Lens Capsule</td>
<td>49</td>
<td>90.74%</td>
</tr>
<tr>
<td>Pupillary margin</td>
<td>39</td>
<td>72.22%</td>
</tr>
<tr>
<td>Iris surface</td>
<td>6</td>
<td>11.11%</td>
</tr>
<tr>
<td>Corneal endothelium</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

PXF - pseudoexfoliation
5) Clinical features of PXF
A significant proportion of eyes with PXF had iris atrophy, sluggish pupil reaction, pupillary dilation less than 0.7mm, subluxated lens, and cup disc ratio more than 0.5 when compared to eyes without PXF (Table 2).

Table 2: Comparison of distribution of clinical characteristics in eyes with versus without pseudoexfoliation.

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Clinical characteristics</th>
<th>Frequency in eyes with PXF (%)</th>
<th>Frequency in eyes without PXF (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Iris atrophy</td>
<td>2 (3.7%)</td>
<td>0</td>
<td>0.02</td>
</tr>
<tr>
<td>2.</td>
<td>Hypopigmented iris</td>
<td>2 (3.7%)</td>
<td>2 (0.8%)</td>
<td>0.094</td>
</tr>
<tr>
<td>3.</td>
<td>Sluggish pupil reaction</td>
<td>12 (22.2%)</td>
<td>2 (0.8%)</td>
<td>0.001</td>
</tr>
<tr>
<td>4.</td>
<td>Dilated pupil &lt; 7mm</td>
<td>21 (38.9%)</td>
<td>1 (0.4%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>5.</td>
<td>Nuclear sclerosis&gt;grade III</td>
<td>38 (70.4%)</td>
<td>129 (52.5%)</td>
<td>0.16</td>
</tr>
<tr>
<td>6.</td>
<td>Mature cataract</td>
<td>13 (24.07%)</td>
<td>48 (19.5%)</td>
<td>0.652</td>
</tr>
<tr>
<td>7.</td>
<td>Subluxated lens</td>
<td>3 (5.6%)</td>
<td>1 (0.4%)</td>
<td>0.003</td>
</tr>
<tr>
<td>8.</td>
<td>IOP ≥ 20mm Hg</td>
<td>8 (14.8%)</td>
<td>9 (3.7%)</td>
<td>0.001</td>
</tr>
<tr>
<td>9.</td>
<td>CCT &lt;500 µ</td>
<td>14 (25.9%)</td>
<td>13 (5.3%)</td>
<td>0.0002</td>
</tr>
<tr>
<td>10.</td>
<td>Endothelial count &lt; 2000</td>
<td>27 (50%)</td>
<td>36 (14.6%)</td>
<td>0.001</td>
</tr>
<tr>
<td>11.</td>
<td>CDR &gt;0.5</td>
<td>17 (31.5%)</td>
<td>29 (11.8%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

PXF – pseudoexfoliation, IOP – intra ocular pressure, CCT – central corneal thickness, CDR – cup disc ratio

6) Central corneal thickness in PXF
The mean CCT was low in patients with PXF i.e; 517microns as compared to 529microns in patients without PXF with a P value 0.001. Significant proportion of eyes with PXF had CCT less than 500 (25.9%) (Table 3).

Table 3: Relation between central corneal thickness and pseudoexfoliation.

<table>
<thead>
<tr>
<th>Central corneal thickness (µ)</th>
<th>&lt;500</th>
<th>500-530</th>
<th>530-550</th>
<th>&gt;550</th>
</tr>
</thead>
<tbody>
<tr>
<td>With no PXF</td>
<td>13 (5.3%)</td>
<td>79 (32.1%)</td>
<td>149 (60.6%)</td>
<td>5 (2.0%)</td>
</tr>
<tr>
<td>With PXF</td>
<td>14 (25.9%)</td>
<td>15 (27.8%)</td>
<td>21 (38.9%)</td>
<td>4 (7.4%)</td>
</tr>
</tbody>
</table>

P= 0.0002 , PXF - pseudoexfoliation

7) Endothelial count in PXF
The mean endothelial count was less in eyes with PXF i.e; 2035 as compared to those without PXF i.e; 2200 with a significance of 0.05. (Table 4)

Table 4: Relation between PXF and endothelial count.

<table>
<thead>
<tr>
<th>Endothelial count</th>
<th>&lt;1700</th>
<th>1700-2000</th>
<th>&gt;2000</th>
</tr>
</thead>
<tbody>
<tr>
<td>With no PXF</td>
<td>2 (0.8%)</td>
<td>34 (13.8%)</td>
<td>210 (85.4%)</td>
</tr>
<tr>
<td>With PXF</td>
<td>5 (9.3%)</td>
<td>22 (40.7%)</td>
<td>27 (50.0%)</td>
</tr>
</tbody>
</table>

P= 0.001, PXF - pseudoexfoliation

8) Optic nerve head in PXF
Cup disc ratio (CDR) was seen to be >0.5 in17 (31.5%) eyes with PXF with a significance of 0.001(Table 2). Out of the 31.5% about 5.6% of PXF had CDR >0.7. But none of these patients were known to be glaucomatous earlier and not on any treatment.

DISCUSSION
The prevalence of pseudoexfoliation vary from region to region (due to the environmental changes) even within a country. The prevalence of PXF among cataract patients attending an eye camp at Kashmir was 26.3%. The prevalence of pseudoexfoliation syndrome in south India was 3.08% in Krishnas et al study, while in Andhra Pradesh eye disease study it was 3.01%. But this low prevalence was among the general population aged above 40 years and not among cataract patients. No studies showed prevalence of PXF among cataract patients in south India. In the present study, among the 300 cataract patients in a tertiary care centre in south India, the prevalence of PXF was 18% (54eyes), which is a significant number as the condition can be missed if not examined under slit lamp carefully. The prevalence is even higher as patients posted for combined surgery and those not satisfying inclusion criteria were excluded). Different studies prove that prevalence of PXF markedly increases with age. The prevalence of PXF markedly increases with age and those not satisfying inclusion criteria were excluded. Different studies prove that prevalence of PXF markedly increases with age. In the present study the age group of patients with PXF ranged from 53 to 82 years and proportion of eyes with PXF increased with age but significance could not be attained .
the male to female ratio was higher in eyes with PXF (28:26 ie; 1.07:1) as compared to patients without PXF (113:133 ie; 0.84 :1).

PXF material can be seen deposited anywhere from corneal endothelium to angle, iris surface, pupillary margin and anterior lens capsule. In our study majority of eyes had deposits over anterior lens surface (90.74%) with 53.7% having it over pupillary margin and anterior lens surface, 29.6% over anterior surface of lens alone and 7.4% over lens capsule, iris and pupillary margin. But none of them had it over corneal endothelium.

This study gave no significant relation between comorbidities like diabetes, hypertension or coronary artery disease (CAD) and pseudoexfoliation. But hypertension and CAD was found in greater proportion in PXF patients as compared to those without PXF. Hypertension was found in 42.5% of eyes with PXF as compared to 30.5% of eyes without PXF. CAD was found in 16.6% of eyes with PXF as compared to 11.1% of eyes without PXF. Diabetes was found in lower proportion 27.7% in eyes with PXF as compared to 31.7% eyes without PXF.

There was no significant difference between the pupillary size before dilation among the two groups. Both the groups had mean pupillary size of 3mm. In Pranathi et al study the most frequent problem encountered was a rigid pupil and none of the pupil with PXF dilated to more than 7mm. Bengal S et al study showed poor pupillary dilatation among 26% of PXF.[10] In the present study also the most frequent complication was poor pupillary dilatation. When the mean dilatation of pupil in patients without PXF was 8.6mm, those with PXF had dilatation of only 6.9mm with a significance of 0.01 and 95% confidence interval of 1.46 – 1.915. PXF eyes had pupillary dilatation less than 7mm in 38.9%, but only 0.4% of the eyes without PXF had poor dilation (\(P = 0.00025\)). Of PXF eyes 22.2% had sluggish reaction to direct pupil reflex as compared to 0.8% eyes without PXF (\(P = 0.001\)). None of the eyes were non reacting to light. Sphincter atrophy may cause sluggish pupillary reactions. But only 3.7% of PXF had significant iris stromal atrophy on slit lamp examination (\(P = 0.02\)). So iris sphincter atrophy is more common than stromal atrophy. This proves the significance of assessing pupillary dilatation prior to surgery so that sufficient measures can be undertaken to prevent complications. Iris hypoxia is associated with hypopigmentation and atrophy of iris pigment epithelium, stroma and muscles which may lead onto poor mydriasis.[9] 3.7% of those with PXF had hypopigmented iris when only 0.8% of eyes without PXF had iris hypopigmentation. Hypopigmentation was uniform throughout involving mainly inner two thirds of the iris.

In Summanen et al study the incidence of cataract formation (nuclear sclerosis) is high in patients with PXF.[11] In the present study also the proportion of eyes with NS III-IV was high in eyes with PXF ie; 70.4% (40.7% had nucleus of grade IV) as compared to eyes without PXF (52.5%). Also the proportion of eyes with mature cataract was also high in eyes with PXF (24.07%) as compared to eyes without PXF(19.5%). This could be due to the increased age of patients with PXF. Lens subluxation was seen in 6.9% of the cases and dislocation in 4.2% of the cases in Yeshigeta et al study.[12] This spontaneous subluxation of lens is due to the zonular weakness. In this study lens subluxation was seen in 5.6% ie; 3 eyes with PXF (all three had mature cataract). A thorough examination under slit lamp for phacodonesis can diagnose this condition.

The frequency of glaucoma vary in different studies. The prevalence of ocular hypertension (intraocular pressure greater than 22 mm Hg but no cupping or field loss) and glaucoma in Kozart et al study is 15% and 7% respectively.[13] and in Andrapradesh eye study is 9.3% and 5.5%.[8] In the present study 14.8% eyes with PXF showed IOP greater than 20mm Hg, with the highest recording being 24mmHg. 31.5% had glaucomatous optic disc changes (CDR >0.5) with about 5.6% having CDR >0.7. Thus nearly only 50% of patients with optic neuropathy had high IOP. This may be due to the marked diurnal fluctuation of IOP in pseudoexfoliation glaucoma (PXG), (one time IOP measurement was only done) causing significant optic neuropathy. This result is consistent with Henry et al study according to which PXG develops in approximately 50% of patients with PXF syndrome over time and is recognized as the most common type of secondary open angle glaucoma.[14] Only newly detected cases of glaucoma were included in our study, implies the actual proportion of PXG is much greater.

Endothelium of the eyes with PXF syndrome show significantly low cell density, with polymegathism and pleomorphism and can serve as early sign of pseudoexfoliation.[15] In the present study though slit lamp examination revealed no PXF deposits over corneal endothelium, the mean endothelial count (measured in cells /mm²) was less in eyes with PXF ie; 2035 as compared to those without PXF ie; 2200. About 9.3% of PXF eyes had very low endothelial count of <1700 and 40.7% had it in the range 1700-2000. So in PXF patients sufficient care must be taken during cataract surgery to prevent further endothelial damage. According to Cankaya et al study the central corneal thickness may not vary among patients with pseudoexfoliation as compared to those without the syndrome.[16] But according to Kirgiz et al study CCT was less in eyes with PXF.[17] The present study was in accordance with the Kirgiz et al study and showed that the mean CCT was low in patients with PXF ie; 517 microns as compared to 529 microns in those without PXF. 53.7% eyes with PXF had CCT <530 microns, of which 25.9% had CCT <500 microns. This low CCT could be another reason for the falsely low IOP recorded.
Since the prevalence of the condition in the population is low, a larger sample size would have yielded better results. Including CCT corrected IOP and studying diurnal variation in IOP could further refine the results.

CONCLUSION
A significant proportion (18%) of eyes posted for cataract surgery have PXF. Low endothelial count and poor pupillary dilation are the most common clinical features. These along with a high grade nuclear sclerosis and / or subluxated lens can make a simple cataract surgery a nightmare. Of the newly detected PXF cases 31.5% had glaucoma related optic neuropathy that makes lifetime follow up and treatment necessary. So awareness and thorough slit lamp examination for PXF is mandatory before proceeding with cataract surgery.

REFERENCES