PATTERN OF PSEUDOEXFOLIATION SYNDROME IN LOWER TO MID HIMALAYAN REGION OF SHIMLA HILLS IN INDIA
P.D. Sharma¹, Yogesh Kumar², R.N. Shasni³

HOW TO CITE THIS ARTICLE:

ABSTRACT: PURPOSE: To study the prevalence and pattern of pseudo-exfoliation syndrome and its complications in lower to mid Himalayan region of Shimla Hills in India. MATERIALS AND METHODS: Thousand consecutive individuals aged ≥40 years visiting outpatient department were subjected to detailed ocular examination for signs of pseudoexfoliation. Intraocular pressure was recorded and pupils were dilated to examine retroiridial anterior lens capsule. Detailed glaucoma work-up was carried out if intraocular pressure was ≥22 mm Hg. RESULTS: Ninety-three out of 1000 individuals examined were diagnosed with pseudoexfoliation syndrome. The prevalence was highest in males, and ≥80 years group, and was increasing with age. The mean age for occurrence in males and females was 65.1±9.2 and 62.3±8.98 years, respectively. Bilateral involvement was more common than unilateral (4.8:1). Pseudo-exfoliation material on anterior lens capsule, seen after dilatation of pupil, was noticed as the commonest sign (91.7% eyes) followed by material on pupillary border (84.7%). Glaucoma capsulare was observed as most common (18.8% eyes) complication followed by phacodonesis and rubeosisiridis. Incidence of unilateral glaucoma capsulare was more common than bilateral, and was statistically significant (Χ²=P, 0.05). A statistically significant relationship was established between the number of pseudo-exfoliation signs, reduction in angle width, and raised intraocular pressure (t=1.32, P<0.1). Incidence of cataract was more in patients with pseudo-exfoliation syndrome than without it. CONCLUSION: Pseudoexfoliation is more prevalent in Shimla hills than rest of India and some other parts of world, but lower than Scandinavian region. Prevalence of glaucoma and senile cataract is significantly higher in pseudoexfoliation. KEY WORDS: Flaky material, glaucoma capsulare, pseudoexfoliation, rubeosisiridis.

INTRODUCTION: Pseudo-exfoliation syndrome (PES) is a complex ocular degenerative disorder characterized by production and progressive accumulation of flaky dandruff like material all over the anterior segment of eye, which may also involve visceral organs.¹ It is recognized as a disease of abnormal basement membrane of the eye.² ³ Characteristic presentation includes deposition of amyloid-like material and pigment on anterior lens capsule, pupillary margin, ciliary body, zonules, corneal endothelium and trabecular meshwork.⁴ ⁵ Anterior to Schwalbe's line, a characteristic pigment deposition called Sampaolesi's line is generally seen.¹ The pigment is released from iris possibly by rubbing against the flaky deposits on lens capsule.⁶ The material is produced by various intraocular tissues and may be an indicator of impaired cellular protection mechanisms.⁷

The disorder has insidious onset, prolonged course, and is the most identifiable cause of pseudoexfoliation glaucoma (PXG) which results due to clogging of trabecular meshwork, juxtacanalicular spaces and Schlemm’s canal by pseudoexfoliation material (PXM) and pigment.
granules.\textsuperscript{5, 6} Other complications include subluxation and dislocation of lens, andrubeosisiridis (iris neovascularisation).\textsuperscript{1}

The distribution of pseudo-exfoliation syndrome is worldwide but prevalence varies depending upon a complex mix of geographical, racial, ethnical and occupational factors. High prevalence has been reported from some parts of the world.\textsuperscript{8-11} In India, prevalence of PES varies from 1.9 \% to 7.4\%.\textsuperscript{12, 13} Shimla Hills are situated in lower to mid Himalayan region of North India at an altitude of 1600 to 2500 metres approximately. This study was therefore aimed at epidemiology of PES in out-door patients visiting our institute.

**MATERIALS AND METHODS:** One-thousand consecutive patients, aged $\geq 40$ years, visiting the ophthalmic department of Indira Gandhi Medical College Hospital, Shimla for sub-normal vision due to cataract or refractive errors were recruited for the study. Patients having traumatic, infective or inflammatory ocular conditions were excluded. Cases of PES with posterior synechiae, insufficiently dilating pupil, and pseudophakia or aphakia after extracapsular cataract extraction (ECCE) were also excluded. Visual acuity was recorded and signs of PES like greyish white flaky deposits on pupillary margin, anterior capsule of lens, zonules if visible and anterior hyaloid (in aphakes) were looked for. Pigment dispersion over posterior surface of cornea, anterior capsule of lens and iris atrophic patches were noted. Intraocular pressure (IOP) of both eyes was recorded with applanation tonometer after anaesthetizing cornea with 4\% xylocaine drops. Gonioscopy was performed to look for PXM and pigment deposits over trabecular meshwork, for Sampaolesi’s line and anterior chamber angle width as per classification by Shaffer.\textsuperscript{14} Pupils were then dilated with phenylepherine (10\%) and tropicamide (1\%) drops. The eyes were re-examined for deposits of PXM and pigment over the retro-iridial portion of anterior lens capsule, zonules if visible, and anterior hyaloid in aphakes. Iridodonesis, phacodonesis, cataract or lens displacement were noted. Optic disc and retina were evaluated and glaucoma suspects were subjected to complete glaucoma work-up.

The guidelines of the Declaration of Helsinki were adhered to, and the study was conducted with informed consent of the participants after approval by the institutional ethics committee.

**RESULTS:** Out of 1000 individuals examined, 572 (57.2\%) were males and 428 (42.8\%) were females. Ninety three (9.3\%) showed varying degree of PES in one or both eyes with a total of 170 eyes being affected. Prevalence was more in males (11.7\%) than females (6.07\%), with highest male (26.4\%) and female (25 \%) prevalence in 70-79 and $\geq 80$ years age groups, respectively.[Table 1] Bilateral manifestation was seen in 77 (82.8\%), and unilateral in 16 (17.2\%) individuals. With advancing age, unilateral to bilateral manifestation was found to increase.[Table 2]

Most common sign of PES was pseudoexfoliation material (PXM) on anterior capsule of lens (91.7\% eyes) followed by PXM on pupillary margin (84.7\% eyes). Phacodonesis, rubeosisiridis, PXM on zonules and subluxated lens were also observed in few patients.[Table 3]

Thirty two (18.8\%) eyes (24 patients) had pseudoexfoliation glaucoma (PXG) while 3 (1.76\%) had ocular hypertension (OH).[Table 4] PXG was more common in females than males. Unilateral glaucoma (16 cases) was twice more common than bilateral (8 cases). Eleven (34.4\%) eyes with PXG also had senile cataract.

Visual acuity in PXG was generally poor; majority (65.6\% of PXG eyes) had just perception of light to nil vision and only2 (6.3 \%) eyes had 6/24 or better vision.[Figure 1]
Prevalence of glaucoma was higher in patients with PES (93 patients) than without it (907 patients). Twenty four (25.8%) patients with PEX showed glaucoma in at least one eye compared to 34(3.7%) patients without PEX. Similarly, senile cataract changes were seen in 67(72.0%) patients with PEX in comparison to 370(40.8%) individuals without PES.[Figure.2]

DISCUSSION: Pseudoexfoliation syndrome is seen worldwide, although prevalence is found to vary. High prevalence has been reported from Scandinavia and Iceland (about 25%), and Finland (over 20%) in patients ≥ 60 years while prevalence in Norway and Sweden was about one-third of that. In Saudi Arabia also, Summanen et al reported high prevalence (13%) of PES. However, no case has been reported in Eskimos. Varying with age, Taylor et al found prevalence of 1.3% to 16% in Australian aborigines. Ritch attributed these wide variations to factors like race, ethnicity, age and sex of population group examined, clinical criteria of diagnosis of exfoliation syndrome, the ability of examiner to detect subtle manifestations of PES in early stages and thoroughness of examination. Many cases go undetected because of failure to dilate the pupils or to examine on slit-lamp after dilation, and because of a low index of suspicion.

In this Himalayan region, cold climate with good sunshine prevails for better part of the year against longer hot periods in most regions of India. Therefore, variation in prevalence of PES was anticipated. We found 9.3% prevalence of PES in hospital visiting population aged ≥ 40.[Table 1] Comparable prevalence of 9% has been reported by Sood et al, while in other parts of India, reported range is 2 to 8 %, since most of the studies have been conducted in ≥ 50 or ≥ 60 years of age, the comparable prevalence in this study turned out to be 10.2% and 12.2%, respectively. The higher prevalence rate could be due to the factors like high-altitude, solar radiation and ethnic characteristics of population. Taylor has implicated solar radiation and occupation as etiological factors. Mohammed et al found greater prevalence of PES in tribals living in mountainous regions of Pakistan than those in lowland valleys. Forsius also observed exfoliation syndrome to be more common in men in populations with high ultraviolet exposure including Yugoslavs, Australian aborigines, Peruvian and Asian Indians. Taylor et al have reported the higher mean ages of patients having PES in older individuals is as low as 0% in Eskimos to as high as 38% in Navajo Indians. With advancing age, we found the prevalence increased markedly from 1.1% in age group 40–49 to 7.6% in 50–59, and 22.2% in ≥ 80 years. Many authors have made nearly similar observations. In Finnish population, PES was reported 10% in aged 60–69 years, 21% in 70–79, and 33% in 80–89. Arsæll A et al also found significantly greater prevalence with age, varying from 2.5% in 50–59 years age group to 40.6% in ≥ 80 years. Forsius observed PES incidence to double every decade after 50 years.

Authors are divided in opinion about predominance of PES in either sex. Male predominance was observed by Yalaz and many other authors. We also found higher prevalence in males (11.7%) than females (6.1%) in the ratio of 1.9:1[Table 1], with significant difference (χ², p<0.05).
However, some studies have shown higher prevalence in females, while few others had no sex variation. Pseudoexfoliation is essentially a bilateral disorder. Initially, one eye may be affected but over the time, it becomes bilateral. In the present study, bilateral predominance was seen in all age groups. Overall, bilateral presentation (82.8%) was nearly five times the unilateral (17.3%) involvement. As the age advanced, there was a shift towards bilaterality: 66.7% in age group 40-49 to 100% in ≥ 80 years. Most authors agree that unilateral cases of PES convert to bilateral over time.

It is the flaky dandruff like material on pupillary margin that alerts the examiner about PES on slit-lamp biomicroscopy. We detected this sign in 144(84.7%) eyes. However, on pupillary dilation, the PXM was seen more commonly on anterior lens capsule (91.7% eyes) than on pupillary margin. Many authors have made similar observations. Therefore, some cases of PES can be missed unless pupils are dilated to examine retroiridial anterior lens capsule. Other signs commonly observed were pupillary ruff degranulation, trabecular-meshwork pigmentation, Sampaolesi’s line and pigment over corneal endothelium. The pigment deposition was diffuse and wide spread. Sugar et al and Prince et al have described similar incidence and pattern of pigment dispersion.

Out of 10 eyes with congenital/surgical coloboma or lens subluxation, in which zonules could be visualised, eight (80%) eyes revealed PXM over zonules. Mizuno reported 100% incidence of pseudo-exfoliation material over zonules and ciliary body on cycloscopic examination. Our observation was based on clinical examination only, yet showed higher incidence. Nearly same incidence (84.6% of aphakic eyes) of PXM on anterior hyaloid surface in aphakic (13) eyes (ICCE performed long ago) was observed. Phacodonesis was seen in 14(8.2%) eyes, probably occurring as a result of weaken and brittle zonules due to enzymatic degradation. Rubeosisiridis was also seen in 4(2.4%) eyes.

PEX-glaucoma (PXG), the most important complication, was observed in 32(18.8%) eyes while ocular hypertension (OH) in 3(1.76%) of the eyes with PES. The reported figures are 9% and 1.7% by Lamba et al, and 7% and 15% by Kozart et al, respectively. However, Klemetti found PXG in only 4% and OH in 44% eyes. Low figures of OH in comparison to PXG in the present study and that by Lamba et al could be due to the fact that in Indian milieu, patients report very late to an ophthalmic center, by which time considerable number of OH patients convert to manifest glaucoma. Moreover, the conversion of ocular hypertensives with PES to glaucoma was found to be more common than that of ocular hypertensives without PES.

In present study, mean age of involvement by PXG was 63.04±7.4 years, which compares well with the findings of Shimizu et al. However, a higher mean age of 69 and 75.6 years has been reported by Smithand Pohjanpelto. The prevalence of PXG is reportedly higher in females than males. Present study showed 34.6% (9/26) prevalence of PXG in females with PES, and 22.38% (15/67) in males with PES, having a ratio of 1.5:1. Two third (66.67%) of them had unilateral while rest had bilateral glaucoma. Hiller et al observed comparable figures of 69% and 31%, respectively. Kozart et al also found unilateral glaucoma (76%) more commonly than bilateral glaucoma (24%).

Higher IOP has been recorded in PXG patients as compared to primary open angle glaucoma (POAG). Christopher et al stated that IOP tends to escalate faster in patients with
pseudoexfoliation glaucoma than primary open-angle glaucoma.\textsuperscript{39} We also found higher mean IOP of 39.5±12.8 mm Hg in PXG eyes. Klemetti, and Kozart et al have concluded that minute pigment granules of PXM cause more severe blockade of aqueous draining channels in PES than POAG.\textsuperscript{25,35}

PXG has worse prognosis than POAG because of higher IOP and poor response to medication, resulting in more severe and faster damage to optic nerve and visual fields. These effects culminate into poor vision. Summanen et al have reported poor to worse vision in 35% eyes in PXG.\textsuperscript{16} In the present study, patients with PXG also had very poor vision; only two (6.2%) eyes had 6/24 or better vision, 20 (62.4%) were economically blind and 10 (31.2%) eyes had no light perception. [Figure 1]

Patients with PES are not only at increased risk of developing glaucoma but also senile cataract.\textsuperscript{39} Topouzis et al found 15.2% prevalence of glaucoma in PES and 4.7% in those without PES.\textsuperscript{40} In comparison, in the present study, the prevalence of PXG was much higher, although that of POAG in non-PES patients was not much different. The prevalence of glaucoma in patients with PES was 25.8% compared to meagre 3.8% (POAG) in those without PES [Figure 2] which was highly significant (z score 8.412, \( p < 0.01 \)). Similarly, senile cataract was found in 67 (77.4%) of patients with PES in comparison to 370 (40.6%) patients having cataract without PES [Figure 2], and the difference was highly significant (z score 4.342, \( p < 0.01 \)). Thus PES patients were nearly two times more prone to senile cataract than those without it, which indicates a probable etiological association of cataract and PES. Since both are essentially age related degenerative disorders, it is possible that co-existence of the latter leads to aggravation of the former. Association of senile cataract with PES has been observed by Layden et al and Mohammed et al as well.\textsuperscript{19,21} Such patients as this are more prone to various complications at the time of cataract surgery.\textsuperscript{39}

It must be born in mind that in POAG, pseudoexfoliation may be a coincidental finding, not responsible for raised intraocular pressure per se. However delineation of such cases has not attempted routinely as it requires elaborate genetic profiling procedures not yet considered foolproof.

**CONCLUSION:** Prevalence of pseudoexfoliation syndrome in OPD-visiting normal population is high in Shimla Hills perhaps due to more ultraviolet radiation and geo-climatic conditions. However clinical features are not very different than most of other studies. Prevalence of pseudoexfoliation glaucoma is considerably higher than generally mentioned. Heightened awareness of clinical signs of PES and PXG is therefore important for early detection and effective management of the disorder to prevent profound visual morbidity. Since incidence of senile cataract is nearly two folds in patients with PES than non-PES patients, it further aggravates visual disability in this disorder. Furthermore, the patients with pseudoexfoliation are at increased risk of cataract surgery related complications.

**REFERENCES:**


<table>
<thead>
<tr>
<th>Age Group (Years)</th>
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<th></th>
<th>Females</th>
<th></th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>n (%)</td>
<td>N</td>
<td>n (%)</td>
<td>N</td>
</tr>
<tr>
<td>40-49</td>
<td>156</td>
<td>2 (1.3)</td>
<td>117</td>
<td>1 (0.8)</td>
<td>273</td>
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<tr>
<td>50-59</td>
<td>155</td>
<td>14 (9)</td>
<td>120</td>
<td>6 (5.8)</td>
<td>275</td>
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<tr>
<td>60-69</td>
<td>155</td>
<td>24 (15.5)</td>
<td>126</td>
<td>14 (11.1)</td>
<td>281</td>
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<tr>
<td>70-79</td>
<td>87</td>
<td>23 (26.4)</td>
<td>57</td>
<td>3 (5.1)</td>
<td>144</td>
</tr>
<tr>
<td>≥80</td>
<td>19</td>
<td>4 (21.1)</td>
<td>8</td>
<td>2 (25)</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>572(57.2)</td>
<td>67 (11.7)</td>
<td>428(42.8)</td>
<td>26 (6.1)</td>
<td>1000</td>
</tr>
<tr>
<td>Mean age</td>
<td>65.1+9.2</td>
<td>------</td>
<td>62.3+8.9</td>
<td>------</td>
<td>64.4+9.2</td>
</tr>
</tbody>
</table>

Table 1: Age and sex-wise prevalence of pseudo-exfoliation syndrome (PES)

Prevalence in Males : Females= 67/572: 26/428 = 1.9 : 1
N= total number of individuals examined in particular age group.
n = number of patients having PES.
%= percentage of patients having PES out of total individuals of the particular group (age and sex-wise) examined.
### Age group (years) vs No. of PES cases

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>No. of PES cases</th>
<th>Unilateral n (%)</th>
<th>Bilateral n (%)</th>
<th>Ratio B/L:U/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>3</td>
<td>1 (33.4)</td>
<td>2 (66.6)</td>
<td>2:1</td>
</tr>
<tr>
<td>50-59</td>
<td>20</td>
<td>5 (25.0)</td>
<td>15 (75.0)</td>
<td>3:1</td>
</tr>
<tr>
<td>60-69</td>
<td>38</td>
<td>7 (18.4)</td>
<td>31 (81.6)</td>
<td>4.4:1</td>
</tr>
<tr>
<td>70-79</td>
<td>26</td>
<td>3 (11.5)</td>
<td>23 (88.5)</td>
<td>7.7:1</td>
</tr>
<tr>
<td>≥80</td>
<td>6</td>
<td>0 (0)</td>
<td>6 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>93</td>
<td>16 (17.2)</td>
<td>77 (82.8)</td>
<td>4.8:1</td>
</tr>
</tbody>
</table>

**Mean age** 60.28 + 8.2 | 65.03 + 9.2

**Table 2: Relationship of age to laterality in pseudo-exfoliation syndrome**

% = percentage of individuals with unilateral/bilateral involvement among total cases of PES in respective groups.

B/L:U/L = bilateral: unilateral cases.

### Signs of pseudo-exfoliation syndrome in 170 Eyes

<table>
<thead>
<tr>
<th>S.No</th>
<th>Signs</th>
<th>No. of Eyes</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>PEX on anterior capsule of lens (pupil dilated)</td>
<td>156</td>
<td>91.7</td>
</tr>
<tr>
<td>2.</td>
<td>PEX on pupillary margin (undilated pupil)</td>
<td>144</td>
<td>84.7</td>
</tr>
<tr>
<td>3.</td>
<td>Degranulation of pupillary ruff</td>
<td>127</td>
<td>74.7</td>
</tr>
<tr>
<td>4.</td>
<td>Pigment deposition on Trabeculum</td>
<td>105</td>
<td>61.7</td>
</tr>
<tr>
<td>5.</td>
<td>Pseudo-exfoliation at angle</td>
<td>82</td>
<td>48.2</td>
</tr>
<tr>
<td>6.</td>
<td>Pigment on corneal Endothelium</td>
<td>84</td>
<td>49.4</td>
</tr>
<tr>
<td>7.</td>
<td>Sampaolesi’s line</td>
<td>80</td>
<td>47.5</td>
</tr>
<tr>
<td>8.</td>
<td>Pigment on anterior surface of lens</td>
<td>56</td>
<td>32.9</td>
</tr>
<tr>
<td>9.</td>
<td>Phacodonesis</td>
<td>14</td>
<td>8.23</td>
</tr>
<tr>
<td>10.</td>
<td>Rubeosislrides</td>
<td>4</td>
<td>2.35</td>
</tr>
<tr>
<td>11.</td>
<td>PEX on anterior hyaloid (ICCE)</td>
<td>11/13 eyes</td>
<td>84.6**</td>
</tr>
<tr>
<td>12.</td>
<td>PEX on Zonule*</td>
<td>8/10 eyes</td>
<td>80.0**</td>
</tr>
</tbody>
</table>

**Table 3: Signs of pseudo-exfoliation syndrome in 170 Eyes**

% = percentage of eyes with particular sign out of total 170 eyes having PES except **

‘Subluxated lens – 2, Congenital iris coloboma - 1, surgical iris coloboma – 5

**percent of 13 and 10 eyes, not 170 eyes

### IOP

<table>
<thead>
<tr>
<th>IOP</th>
<th>No. of eyes</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (≤ 22 mm Hg with normal optic cup and visual fields)</td>
<td>135</td>
<td>79.4</td>
</tr>
<tr>
<td>Ocular Hypertension (&gt; 22 mm Hg with normal optic cup and visual fields)</td>
<td>3</td>
<td>1.8</td>
</tr>
<tr>
<td>Glaucoma (&gt; 22 mm Hg with enlarged optic cup and visual field defects)</td>
<td>32</td>
<td>18.8</td>
</tr>
<tr>
<td>Total eyes of 93 individuals with PES</td>
<td>170</td>
<td>100</td>
</tr>
</tbody>
</table>

**Table 4: IOP Status in 170 eyes (93 individuals) with PES**

Mean Age - 63.04 + 7.4 years, mean IOP- 39.5 + 12.8 mm of Hg,
Prevalence of PXG in Females with PES: Males with PES = 9/26: 15/67 = 1.5:1
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Date of Submission: 27/11/2013.
Date of Peer Review: 29/11/2013.
Date of Acceptance: 10/12/2013.
Date of Publishing: 24/12/2013.