

## SCIENTIFIC REPORT

## Pseudoexfoliation in south India

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**Aim:** To study the profile of pseudoexfoliation in a population based study.

**Method:** 2850 consecutive subjects aged 40 years or older from a population based survey in a rural area of southern India underwent complete ophthalmic evaluation including history, visual acuity testing, refraction, slit lamp examination, applanation tonometry, gonioscopy, and dilated examination of the lens (including LOCS II grading of cataract), fundus, and optic disc. Patients with pseudoexfoliation syndrome were identified and their data were analysed with respect to age, sex, intraocular pressure, gonioscopic grading, cataract, and optic neuropathy.

**Results:** 108 subjects had pseudoexfoliation syndrome (3.8%). There was a significant increase in prevalence with age but no sex predilection. The condition was unilateral in 53 cases (49.1%) and bilateral in 55 cases (50.9%). 18 cases with pseudoexfoliation (16.7%) had high intraocular pressure (>21 mm Hg), 16 cases (14.8%) had occludable angles, and 14 cases (13%) had pseudoexfoliation glaucoma. There was a significantly higher prevalence of cataract among people with pseudoexfoliation compared to those without pseudoexfoliation ( $p=0.014$ ).

**Conclusion:** The prevalence of pseudoexfoliation syndrome in the rural population of south India was 3.8%. Raised intraocular pressure was seen in 16.7% of people with pseudoexfoliation and glaucoma was present in 13%.

Pseudoexfoliation (PEX) syndrome is the most common identifiable cause of open angle glaucoma worldwide.<sup>1</sup> It is a generalised disorder of the extracellular matrix characterised by the production of abnormal basement membrane-like material in several intraocular and extraocular tissues. The trigger for the production of PEX material remains to be identified. Clinically, the pseudoexfoliation material can be seen deposited in the anterior segment on the pupillary ruff, the anterior lens capsule, and other anterior segment structures. On the anterior capsule it has a characteristic distribution of a central disc surrounded by a clear zone, surrounded by a peripheral ring-like deposit of granular material. Associated anatomical features include pupillary ruff atrophy, pigment dispersion and, commonly, elevated intraocular pressures with or without glaucoma.<sup>2</sup> It has also been reported to be a risk factor for narrow angles and angle closure glaucoma (ACG).<sup>3,4</sup>

The reported prevalences in different parts of the world have varied from 0% to 38% in different populations.<sup>5–8</sup> There are no population based data on the prevalence of this syndrome from the Indian subcontinent. In this study, we report the prevalence and characteristics of PEX syndrome in a rural population in southern India.

## METHODS

This study is part of an ongoing population based study to estimate the prevalence of glaucoma in a defined geographical

area of rural south India. The target population was identified by selecting a group of 32 geographically contiguous villages in Thiruvallur and Kanchipuram districts of the state of Tamil Nadu in south India. People aged 40 years or above residing in the target area were enumerated, motivated, and the willing people brought to the base hospital for a comprehensive ophthalmic evaluation. The study was carried out after approval by the institutional review board. Written informed consent was obtained from all participants before the commencement of examination. The first consecutive 2850 people who were enrolled and examined between 15 June 2001 and 16 July 2002 were included in this study.

## Eligibility criteria

Those aged 40 years and above or those turning 40 in the current calendar year and resident at the target address for a minimum period of 6 months were eligible for inclusion.

## Exclusion criteria

People staying at the target households for a period of less than 6 months, temporary residents (people who have permanent residence elsewhere), and hostel dwellers were excluded. Very old people and/or invalids who could not be transported to the examination centre were also excluded from the study.

## Examination procedures

The ophthalmic evaluation included recording of relevant ocular and medical history, recording of best corrected visual acuity with logMAR chart, examination of the pupillary reaction, and slit lamp evaluation of the anterior segment with careful search for PEX deposits. Intraocular pressure (IOP) was recorded by Goldmann applanation tonometry. Gonioscopy was performed on all subjects using a Sussmann-type 4 mirror hand held gonioscope (Volk Optical Inc, Mentor, OH, USA). Gonioscopy was first done using a short beam that does not cross the pupil and indentation gonioscopy was performed whenever necessary. Subjects with open angles had their pupils dilated with 5% phenylephrine and 1% tropicamide eye drops. If phenylephrine was contraindicated, 1% homatropine eye drops were used instead. If the angles were found to be occludable the need for laser iridotomy was explained to the subject and it was performed after obtaining the subject's consent. The rest of the examination was deferred to another convenient date following the laser iridotomy.

Repeat slit lamp evaluation was done after dilatation. The anterior lens capsule was examined again for PEX deposits under dilatation. The subject was classified as having PEX syndrome if PEX material was present in either or both eyes. Cataract grading by LOCS II system was done in those patients where the pupil dilated to 6 mm or more.<sup>9</sup> Stereoscopic evaluation of the fundus and the optic disc with the indirect ophthalmoscope and the +78 D lens was performed followed by the optic disc stereophotography.

### Diagnostic criteria

An occludable angle was diagnosed if the pigmented trabecular meshwork was not visible in more than 180° of the angle in dim illumination. Glaucomatous optic nerve damage was diagnosed based on a combination of one or more of the following features: (i) vertical cup-disc ratio of 0.8 or more (physiological cups were excluded); (ii) vertical cup-disc asymmetry of 0.3 or more between the two eyes; (iii) characteristic glaucomatous excavation of the neuroretinal rim. Open angle glaucoma (OAG) was diagnosed on the basis of open angles on gonioscopy with glaucomatous optic nerve damage as described above with corroborative visual field changes when a reliable visual field was obtained. Subjects with intraocular pressure (IOP) >21 mm Hg with healthy optic discs and normal fields were labelled ocular hypertensive (OHT). All subjects with IOP greater than 21 mm Hg and/or suspicious optic disc changes were asked to return for a Humphrey visual field examination. In those for whom visual field data were either not available, or were unreliable, the diagnosis of glaucoma was based entirely on the appearance of the optic disc.

Nuclear colour of NC I or more with nuclear opalescence N2 or more according to the LOCS II system was considered as significant nuclear sclerosis.

### Statistical analysis

Collected data were entered in a database using Microsoft Access software.

For calculation of mean IOP only one eye of each person was considered. In people with unilateral PEX, the eye with PEX was considered. In those with bilateral PEX and in the population without PEX, one eye was chosen at random.

For comparison of nuclear sclerosis, the eye with PEX was chosen for cases with unilateral PEX and one eye was chosen at random for cases with bilateral PEX. From the subjects who did not have PEX, a subset of age matched people was selected for comparison and one eye was chosen at random.

Analysis of data was performed using *t* and 'z' tests and  $\chi^2$  for trend as relevant.

### RESULTS

Of 2850 subjects examined, 108 (3.8%) were found to have PEX syndrome, with unilateral disease in 53 (49.1%) and bilateral in 55 (50.9%) subjects. Of those with unilateral disease, 36 (67.9%) were in the right eye and 17 (32.1%) were in the left eye. The mean age of subjects with PEX was 64.7 (SD 9.63) years while the mean age of subjects without PEX was 53.54 (10.49) years, the difference being significant (*t* test,  $p < 0.001$ ). Table 1 shows the age specific prevalence of PEX syndrome.  $\chi^2$  analysis for trend showed a significant linear increase of PEX with age ( $p < 0.001$ ). The mean age of the unilateral PEX and bilateral PEX subjects was 63.72 (10.11) and 65.66 (9.14) years respectively, the difference being insignificant (*t* test,  $p = 0.143$ ).

Women outnumbered men in the PEX as well as the non-PEX groups. Women constituted 54.6% of subjects with PEX and men constituted 45.4% of them. Among subjects without

PEX, 55.4% were women and 44.6% were men. There was no significant difference in sex distribution between both groups—this remained after adjusting for age ('z' test,  $p = 0.953$ ; age adjusted odds ratio, 1.22; 95% confidence interval, 0.74 to 1.99).

For calculation of mean IOP, only one eye of each person was considered. In people with unilateral PEX, the eye with PEX was considered. In those with bilateral PEX and in the population without PEX, one eye was chosen at random.

The mean IOP in people with PEX was 15.42 (6.12) mm Hg (95% confidence interval, 14.17 to 16.67) and without PEX was 14.13 (3.88) mm Hg (95% confidence interval 13.99 to 14.28) respectively—the difference was significant (*t* test,  $p = 0.001$ ). Eighteen (16.7%) cases with PEX syndrome had IOP higher than 21 mm Hg at presentation; 10 of them were ocular hypertensives (9.3% of PEX). Occludable angles were seen in 16 (14.8%) cases with PEX; 11 of the 94 (11.7%) non-glaucoma subjects with PEX had narrow angles. Disc changes characteristic of glaucoma (PEX glaucoma) were seen in 14 (13%) cases with PEX, six of whom had a normal IOP record at presentation. Of the 14 patients with PEX glaucoma, nine cases had open angles and five had occludable angles on gonioscopy. Twenty five subjects with PEX syndrome were advised to undergo Humphrey visual field testing, of whom only 13 returned for the test. Among the visual field tests performed, only three of them were reliable and they all showed typical arcuate scotomas. Prevalence of OHT, OAG, and occludable angles was significantly higher among people with PEX compared to those without PEX—this difference remained after adjusting for age (Table 2).

Cataract grading by the LOCS II system was available for 79 people in the PEX group. As the mean age of the PEX group was significantly higher than the mean age of subjects without PEX, a subset of 79 age matched people was selected from the non-PEX group for comparison. Fifty three (67.1%) subjects with PEX had significant nuclear sclerosis compared to 43 (54.4%) people without PEX. The difference was significant ('z' test,  $p = 0.014$ ).

### DISCUSSION

The reported prevalence rate of PEX syndrome in different populations shows extensive variations—0% in Eskimos,<sup>5</sup> 1.6% in a south eastern US population,<sup>6</sup> 1.8% in the Framingham Eye Study,<sup>7</sup> 5–25 % in the Scandinavian countries,<sup>5</sup> and 38% in Navajo Indians.<sup>8</sup> More recent population based estimates in Australia reveal prevalences of 0.98% in the Visual Impairment Project<sup>10</sup> and 2.3% in the Blue Mountains Eye Study.<sup>11</sup> These could reflect true variations arising from racial, genetic, and/or geographical differences. Some of the variability could be explained by differences in techniques of assessment and whether PEX was actively looked for with a dilated pupil. However, they could also be accounted for by many other factors including differences in study design (prospective versus retrospective), sampling methods (population based, hospital based, or clinic based), population size, and age distributions in the sampled populations. A literature search revealed only two reports on the prevalence of PEX syndrome in India. The first, by Sood and Ratnaraj in 1968, reported 1.87% prevalence in patients aged 45 years or above with a 34% prevalence of glaucoma in patients with PEX.<sup>12</sup> The last report on the subject is by Lamba and Giridhar in 1984,<sup>13</sup> who reported a 7.4% prevalence of PEX, 9% of whom had glaucoma. Both these were hospital based studies. The current study is the only population based study on PEX syndrome from India.

We found that the mean age of subjects with PEX syndrome is 11.16 years older than the normal population. Considering age specific prevalence rates, there was a significant linear increase in prevalence with age. It is well

**Table 1** Age specific prevalence of PEX syndrome

Age (years)	No of subjects with PEX	Total population	Prevalence (%)
40–49	6	1128	0.53
50–59	19	740	2.57
60–69	43	646	6.66
70–79	33	298	11.07
≥ 80	7	38	18.4

PEX = pseudoexfoliation.  $\chi^2$  analysis for trend:  $p < 0.001$ .

**Table 2** Prevalence of occludable angles in people with and without pseudoexfoliation (PEX) syndrome

	No PEX (2742)*	PEX (108)	p value†	Age adjusted OR (95% CI)
Ocular hypertension	1.24% (34)	9.26% (10)	<0.001	12.94 (5.61 to 29.85)
Open angle glaucoma	1.68% (46)	8.33% (9)	<0.001	2.84 (1.31 to 6.21)
Occludable angles	7.36% (102)	14.81% (16)	0.002	1.96 (1.12 to 3.49)

\*Actual number of subjects given in parentheses, †p value calculated using 'z' test.

known that the prevalence of PEX increases with age.<sup>6-10,11</sup> The bilateral cases were not significantly older than the unilateral cases. These findings are similar to those of other studies.<sup>14</sup> The sex distribution in our study was similar to that of the normal population without any predilection towards either sex, which is also in accordance with other studies,<sup>13</sup> although some studies have reported a female preponderance.<sup>14</sup>

The mean IOP in subjects with PEX was 1.29 mm Hg higher than in those without PEX. This difference was significant, though there was a slight overlap of the 95% confidence intervals. High IOP was recorded in 16.7% of subjects with PEX. Ocular hypertension, that is, high IOP without glaucomatous optic neuropathy, was found in 9.3% of cases with PEX. Glaucomatous optic neuropathy was found in 13% of PEX cases. Almost all studies focusing on PEX in the past have shown an association with raised IOP and glaucoma. Kozart and Yanoff,<sup>14</sup> in a clinic based study of 100 consecutive patients with PEX, reported 15% prevalence of OHT and 7% prevalence of glaucoma. However, raised IOP was necessary for the diagnosis of glaucoma in their study. The Blue Mountains Eye Study,<sup>11</sup> a population based study where the diagnosis of PEX glaucoma was based on optic neuropathy with or without raised IOP, reported 9.3% OHT and 14.2% glaucoma, which are similar to our data. It is known that IOP spikes occur in PEX syndrome that may not manifest on a single IOP record.<sup>15</sup>

We found a 14.8% prevalence of narrow angles in our population with PEX, which is twice the prevalence in our population (Table 2) without PEX. Glaucomatous optic neuropathy was found in 31.3% of our PEX cases with occludable angles (4.6% of all PEX patients). Layden and Schaffer<sup>3</sup> reported a 23% prevalence of narrow angles in 100 patients with PEX. Wishart *et al*<sup>4</sup> reported 18% occludable angles in their 76 patients with PEX. A rigid and sticky iris, a greater tendency to form posterior synechiae, and anterior lens subluxation due to zonular weakness have been thought to predispose to these conditions, which are worsened by miotic therapy.<sup>2</sup> Many studies did not include gonioscopy routinely on all subjects.<sup>11-14</sup> In addition to differences in study design and target populations, variations between previous studies and our study may have been the result of differences in the definition of narrow angles, miotic use in the earlier days when these studies were reported, and true differences in the prevalence of angle closure between the populations.

PEX syndrome has been known to be associated with a greater prevalence of cataract though the exact aetiology of this association is not known.<sup>1-3,16</sup> Our finding that nuclear sclerosis is more prevalent in the PEX population is in accordance with previous studies.

A major drawback of our study was that only 52% of those who were advised to have a Humphrey visual field test returned for the test. Of these, only 12% performed the field test reliably. The population studied was a rural, predominantly illiterate one accounting for the unwillingness to return for a field examination. Jacob *et al* reported a similar

problem in a population based prevalence study of glaucoma from a different population in south India.<sup>17</sup> Poor reliability can also be attributed to the same factors. These factors may have led to underestimation of the prevalence of glaucoma. However, the optic disc was carefully evaluated in all subjects and as disc changes usually precede visual field loss, it is unlikely that the results were altered significantly.

In conclusion, we found a 3.8% prevalence of PEX syndrome in this rural population of south India aged 40 years and above. We found that increased intraocular pressure, occludable angles, and glaucomatous optic neuropathy occur more frequently in the population with PEX syndrome compared to people without PEX.

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