CrossMark

American Academy of Ophthalmology
The Eye M.D. Association

Six-Year Incidence and Baseline Risk Factors for Pseudoexfoliation in a South Indian Population

The Chennai Eye Disease Incidence Study

Lingam Vijaya, MS,[1,] Rashima Asokan, MPhil,[1,2,3] Manish Panday, MS,[1] Nikhil S. Choudhari, DNB,[1] Sathyamangalam Ve Ramesh, PhD,[1,2] Lokapavani Velumuri, MPhil,[1,2] Ronnie George, MS[1,*]*

Objective: To estimate the 6-year incidence of pseudoexfoliation and its risk factors in a South Indian population.

Design: Longitudinal population-based study.

Participants: Subjects 40 years of age or older without pseudoexfoliation at baseline.

Methods: Participants were examined at baseline and after a 6-year interval. The presence of pseudoexfoliation was looked for after pupillary dilation in either or both eyes at 1 or more locations. Glaucoma was defined using the International Society of Geographical and Epidemiological Ophthalmology Classification. Logistic regression was performed to identify the baseline risk factors that could predict the incident pseudoexfoliation.

Main Outcome Measures: Six-year incidence, associated risk factors, and rural-versus-urban differences.

Results: From the study cohort of 4228 subjects, 87 subjects (male-to-female ratio, 48:39; rural-to-urban ratio, 69:18) demonstrated incident pseudoexfoliation (2.03%; 95% confidence interval [CI], 1.6–2.5; rural: −2.86%; 95% CI, 1.6–2.5; urban: 0.96%; 95% CI, 0.5–1.4). Pseudoexfoliation was associated with glaucoma in 1 subject (1.1%), with primary angle-closure suspicion in 10 subjects (11.5%), and with ocular hypertension in 2 subjects (2.2%). Significant predictive baseline risk factors were older age ($P < 0.001$), rural residence ($P < 0.001$), illiteracy ($P = 0.02$), pseudophakia ($P = 0.04$), and nuclear cataract ($P = 0.05$). With reference to the 40-to-49-year age group, the risk of incidence increased from 4.7 (95% CI, 2.4–9.4) for the 50-to-59-year age group to 12.9 (95% CI, 6.1–27.2) for 70 years of age and older group.

Conclusions: In 6 years, pseudoexfoliation developed in 2.03% of the population. Rural and urban incidence was significantly different. *Ophthalmology 2015;122:1158-1164 © 2015 by the American Academy of Ophthalmology.*

Pseudoexfoliation is an age-related generalized disorder of the extracellular matrix that results in the production of an abnormal basement membrane-like material. This material can become deposited in several intraocular and extraocular tissues. In the eye, pseudoexfoliation material tends to accumulate at the pupillary margin, in the angle, and on the anterior lens capsule, zonules, and anterior vitreous. On the anterior capsule, it has a characteristic distribution of a central disc enclosed by a clear zone that is surrounded by a ring-like deposit of the material.[1–3] These deposits lead to clinical conditions such as open-angle glaucoma, angle closure, and instability of zonular support to the lens.[4–6] Not all people with pseudoexfoliation go on to demonstrate glaucoma. In those who do, glaucoma can be difficult to treat.[3] It has been linked to the *lysyl oxidase 1* gene. Lysyl oxidase 1 is an enzyme needed for elastin production and stability and is found in pseudoexfoliation deposits.[7,8] Many population-based cross-sectional studies have reported the prevalence of pseudoexfoliation in different populations. The highest prevalences have been reported from Scandinavian countries and Greece.[9–30] Limited information is available on the incidence of pseudoexfoliation.[31–33] Incidence studies can help to identify possible risk factors for the development of the disease over time. Herein, we report the 6-year incidence of pseudoexfoliation, its associated risk factors, and rural-versus-urban differences in incidence.

Methods

Study Design and Population

The methodology of the Chennai Glaucoma Study was published previously.[34] In brief, the Chennai Glaucoma Study was a cross-sectional population-based study conducted from 2001 through 2004 to measure the prevalence of glaucoma in rural and urban South India. The study cohort consisted of 9600 subjects 40 years of age or older (rural-to-urban ratio,

http://dx.doi.org/10.1016/j.ophtha.2015.02.007
ISSN 0161-6420/15

4800:4800). From the cohort, 7774 subjects participated in the study (rural-to-urban ratio, 3924:3850). Six years later (2007−2010), this cohort was re-examined to assess the incidence of eye diseases in the Chennai Eye Disease Incidence Study. Participants from the baseline cohort were re-enumerated by social workers and invited to undergo a detailed ocular examination at the base hospital. In the case of those who did not respond, the social worker made up to 3 household visits on different days to convince the participants to come for the evaluation. If they did not undergo evaluation despite this, they were considered nonparticipants. The examination protocols were the same for both studies. The institutional review board approved the study. The study was performed after obtaining written informed consent, in accordance with the tenets of the Declaration of Helsinki.

Clinical Examination

All participants who responded underwent a detailed ophthalmic examination at a dedicated facility created at the base hospital. A detailed history pertaining to medical and ophthalmic conditions was elicited. The eye examination consisted of measuring best-corrected visual acuity using logarithm of minimum angle of resolution 4-m charts (Light House Low Vision Products, New York, NY), external examination and pupillary evaluation using a flashlight, slit-lamp biomicroscopy, intraocular pressure (IOP) measurements using a Goldmann applanation tonometer (Zeiss AT 030 Applanation Tonometer; Carl Zeiss, Jena, Germany), gonioscopy using a 4-mirror Sussman lens (Volk Optical, Inc, Mentor, OH), grading of lens opacification at the slit lamp using the Lens Opacities Classification System II with a minimum pupillary dilation of 6 mm, repeat slit-lamp evaluation after dilatation for pseudoexfoliation deposits, detailed retinal examination with a binocular indirect ophthalmoscope using a +20-diopter (D) lens, and stereoscopic evaluation of the optic nerve head using a +78-D lens at the slit lamp. The vertical and horizontal cup-to-disc ratios (CDRs) were measured and recorded. Presence of any local thinning or notching, splinter hemorrhages, and peripapillary atrophy was documented. Central corneal thickness was measured using the DGH 550 ultrasonic pachymeter (DGH Technology, Inc, Exton, PA). Automated visual fields were performed for all the subjects with best-corrected visual acuity of 4/16 or better using the screening C-20-1 program of frequency doubling perimetry (Carl Zeiss Meditec, Inc, Dublin, CA). On gonioscopy, primary angle-closure suspect (PACS) was defined as an angle where the pigmented trabecular meshwork was not visible in more than 180° in dim illumination without indentation. Laser iridotomy was performed in subjects with PACS after obtaining their consent; these patients underwent the rest of examination on another day.

A provisional diagnosis of suspected glaucoma was made when the subject had 1 or more of the following conditions: IOP of 21 mmHg or more in either eye; vertical CDR of 0.7 or more in either eye or CDR asymmetry of 0.2 or more; or focal thinning, notching, or splinter hemorrhage. All these subjects were asked to perform threshold visual field test using the Swedish interactive threshold algorithm standard 24-2 program (model 750; Carl Zeiss Meditec, Inc). A glaucomatous field defect was diagnosed using a single, reliable threshold visual field examination. The field was considered to be abnormal if the glaucoma hemifield test results were outside normal limits and 3 or more abnormal contiguous points were depressed to $P < 0.05$. Reliability criteria were as recommended by the instrument's algorithm (fixation losses, <20%; false-positive and false-negative results, <33%).

Diagnostic Definitions

We diagnosed pseudoexfoliation if exfoliative material was present in 1 or both eyes at 1 or more locations, namely, the pupillary margin, anterior lens capsule, anterior chamber angle, corneal endothelium, anterior vitreous face, and zonules. In the Lens Opacities Classification System II, nuclear cataract is defined as presence of a nuclear sclerosis grade of N2 or more. Cases of glaucoma were defined using the International Society of Geographical and Epidemiologic Ophthalmology classification.[35] Glaucoma was classified according to 3 levels of evidence. In category 1, diagnosis was based on structural and functional evidence. It required CDR or CDR asymmetry in the 97.5th percentile or more for the normal population or a neuroretinal rim width reduced to 0.1 CDR (between 10 and 1 o'clock or 5 and 7 o'clock) with definite visual field defects consistent with glaucoma. Category 2 was based on advanced structural damage with unproven field loss. This included those subjects in whom visual fields could not be performed or for whom they were unreliable, with CDR or CDR asymmetry in the 99.5th percentile or more for the normal population. Finally, category 3 consisted of persons with an IOP of more than the 99.5th percentile for the normal population whose optic discs could not be examined because of media opacities. For the current study population, the 97.5th and 99.5th percentiles were as follows: CDR, 0.7 and 0.8; CDR asymmetry, 0.2 for both; and IOP, 24 and 30 mmHg in the urban population and 21 and 25 mmHg for the rural population.[36,37] An IOP of more than the 97.5th percentile was defined as ocular hypertension. Body mass index (BMI) was defined as weight in kilograms divided by the square of height in meters (kg/m^2). The BMI categories were grouped as underweight (<18.5 kg/m^2), normal (18.5−25 kg/m^2), overweight (>25 kg/m^2), and obese (≥30.0 kg/m^2).

Statistical Analysis

Statistical analysis was performed using SPSS software version 15 (SPSS Inc, Chicago, IL). Subjects were classified into 4 groups based on baseline age: 40 to 49 years, 50 to 59 years, 60 to 69 years, and 70 years or older. Comparison of variables between subjects with and without pseudoexfoliation was performed using the *t* test for continuous variables and the chi-square test for categorical variables. Logistic regression was performed to analyze risk factors such as age, gender, location of residence, IOP, cataract, CCT, BMI, occupation, literacy, smoking, smokeless tobacco use, alcohol consumption, and lens status for the incidence of pseudoexfoliation after adjusting for age, gender, and location of residence. Statistical significance was assessed at a *P* value of less than 0.05, and odds ratios are presented with 95% confidence intervals (CIs).

Results

At baseline, 7774 participants were examined. From this cohort, 1752 subjects (rural-to-urban ratio, 877:875) could not be contacted because they migrated with no forwarding address. Of the 6022 subjects (rural-to-urban ratio, 3047:2975) who could be contacted or for whom information was available, 590 persons were deceased. The final number of eligible subjects was 5432, and 4421 (rural-to-urban ratio, 2510:1911; response rate, 81.3%) were examined. The reasons for nonparticipation were migration (n = 804 [14.8%]), declining to participate (n = 145 [2.7%]), and being bedridden (n = 62 [1.1%]). Table 1 provides the characteristics of participants and nonparticipants. From this cohort of 4421 subjects, we excluded 133 subjects with pseudoexfoliation at baseline and examined 4228 subjects for

Table 1. Comparison of Baseline Characteristics of Participants and Nonparticipants in the Chennai Eye Disease Incidence Study

Parameter Studied	Participants (n = 4421)	Nonparticipants (n = 3353)	P Value
Age (yrs)*	52.8±9.7	56.4±11.3	<0.001
Male-to-female ratio (%)	1972:2449 (44.6:55.4)	1500:1853 (44.7:55.3)	0.46
Rural-to-urban ratio (%)	2510:1911 (56.8:43.2)	1414:1939 (42.2:57.8)	<0.001
Cataract surgery (no:yes; %)	4056:365 (91.7:8.3)	2972:381 (88.6:11.4)	<0.001
Smoking (no:yes; %)	3666:755 (82.9:17.1)	2742:611 (81.8:18.2)	0.19
Smokeless tobacco (no:yes; %)	3714:707 (84.0:16.0)	2847:506 (84.9:15.1)	0.28
Alcoholism (no:yes; %)	3789:632 (85.7:14.3)	2835:518 (84.6:15.4)	0.16
Literate-to-illiterate ratio (%)	2705:1716 (61.2:38.8)	2152:1201 (64.2:35.8)	0.007
Manual-to-nonmanual occupation ratio (%)	2887:1534 (65.3:34.7)	2192:1161 (65.4:34.6)	0.96
CCT (μm)	510.4 (34.9)	511.4 (37.1)	0.19
IOP (mmHg)	15.2 (4.3)	15.5 (4.4)	0.001
PEX (no:yes; %)	4288:133 (97.0:3.0)	3196:157 (95.3:4.7)	<0.001
BMI (%)			0.42
Normal	1179 (26.7)	1088 (32.4)	
Underweight	276 (6.2)	293 (8.7)	
Overweight	637 (14.4)	603 (18.0)	
Obese	234 (5.3)	205 (6.1)	

BMI = body mass index; CCT = central corneal thickness; IOP = intraocular pressure; PEX = pseudoexfoliation.
*Mean±standard deviation.

incident pseudoexfoliation. Eighty-seven subjects (male-to-female ratio, 48:39; rural-to-urban ratio, 69:18) had incident pseudoexfoliation. Of 87 subjects, the diagnosis was based on presence of pseudoexfoliation in a single location in 63 subjects, presence in 2 locations in 23 subjects, and presence in more than 2 locations in 1 subject. The most common location was the anterior lens surface in phakic eyes and the capsular surface in cataract-operated eyes. The crude incidence of pseudoexfoliation was 2.03% (95% CI, 1.6−2.5), and it was 2.86% (95% CI, 1.6−2.5) and 0.96% (95% CI, 0.5−1.4) for the rural and urban populations, respectively. Assuming a linear incidence of pseudoexfoliation, the annual incidence was 0.34%. Of 87 subjects with incident pseudoexfoliation, 1 had pseudoexfoliation with glaucoma (1.1%), 10 had associated PACS (11.5%), and 2 had ocular hypertension (2.2%). The age- and gender-adjusted (to the population of Tamil Nadu) incidence of pseudoexfoliation among subjects 40 years of age and older was 2.34% (95% CI, 2.33−2.36); it was 3.36% (95% CI, 3.33−3.39) in the rural population and 1.1% (95% CI, 1.08−1.12) in the urban population. Adjusted annual incidence was 0.39%.

Comparing those with or without pseudoexfoliation (Table 2), those with pseudoexfoliation were more likely to be older, male, rural residents, smokeless tobacco users, alcohol consumers, and illiterate, to have nuclear cataract and lower BMI, and to be pseudophakic or aphakic. The baseline risk factors (Table 3) that predicted the incident pseudoexfoliation were older age ($P < 0.001$), rural residence ($P < 0.001$), pseudophakia ($P = 0.04$), illiteracy ($P = 0.02$), and nuclear cataract ($P = 0.05$). In comparison with the 40-to-49-year age group, the odds ratio for incident pseudoexfoliation increased from 4.7 (95% CI, 2.4−9.4) for the 50-to-59-year age group to 12.9 (95% CI, 6.1−27.2) for 70 years and older age group. Figure 1 depicts the gradual increase in incident pseudoexfoliation with age; this trend was observed in both rural and urban populations. Adjusted (for residence, age, gender, and smoking status) baseline BMI and CCT did not predict independently the incident pseudoexfoliation. We further analyzed the relationship between BMI and stratification of CCT distribution by the tertiles (<497 μm, 497−<525 μm, >525 μm). The group with lower baseline BMI and thinner CCTs showed the highest incidence of pseudoexfoliation (Fig 2).

Discussion

The Chennai Eye Disease Incidence Study is a longitudinal study from India that provides 6-year eye disease incidence in adults 40 years of age and older. Herein, we report the incidence of pseudoexfoliation. The crude incidence at the 6-year follow-up was 2.03% (95% CI, 1.6−2.5), and the age- and gender-adjusted incidence was 2.34% (95% CI, 2.33−2.36). Our incidence is much lower than the incidence of pseudoexfoliation in Icelanders. The reported 5-year incidence of pseudoexfoliation from Iceland[31] in people 50 years of age and older was 3.5% (right eye) and 5.2% (either eye) compared with 2.5% (4.7% and 1.5% for rural and urban populations) at 6 years for our population older than 50 years. Unlike our study, the previous study excluded all eyes with pseudophakia at baseline and the 5-year follow-up examination. The incidence might have been even higher if they had included those subjects with pseudophakia. In a retrospective population-based study from a white population,[32] the reported adjusted annual incidence of pseudoexfoliation was 0.026% over a 16-year follow-up period, and this is considerably lower than our adjusted annual incidence of 0.39%. Possible reasons for low incidence could be (1) not all patients underwent a dilated examination, so cases of pseudoexfoliation were missed; and (2) during the study period, multiple ophthalmologists examined the patients, so if pseudoexfoliation was not looked for specifically, the diagnosis would have been missed. At this point, the limited information available suggests that the incidence of pseudoexfoliation seems to be variable and possibly more common in certain geographical locations such as Iceland. However, there are large differences in the definitions and methods used among the studies, which also contribute to the variability.

Table 2. Comparison of Participants with and without Incident Pseudoexfoliation in the Chennai Eye Disease Incidence Study

Parameter	Study Population (n = 4288)	Population without Pseudoexfoliation (n = 4201)	Population with Pseudoexfoliation (n = 87)	*P* Value	*P* Value after Excluding Glaucoma Subjects
Age group (yrs; %)				<0.001	<0.001
40–49	967 (22.6)	962 (22.9)	5 (5.7)		
50–59	1532 (35.7)	1512 (35.9)	20 (22.9)		
60–69	1116 (26.0)	1085 (25.8)	31 (35.6)		
70+ (range, 70–91)	673 (15.7)	642 (15.3)	31 (35.6)		
Male-to-female ratio (%)	1897:2391 (44.3:54.8)	1849:2352 (44.2:55.9)	48:39 (55.1:44.8)	0.05	0.03
Rural-to-urban ratio (%)	2415:1873 (56.3:43.7)	2346:1855 (55.8:44.1)	69:18 (79.3:20.7)	<0.001	<0.001
IOP*	14.2±3.9	14.2±3.9	13.9±4.3	0.56	0.08
CCT*	509.9±71.3	510.2±71.9	499.8±33.4	0.19	0.91
Nuclear cataract (no:yes; %)	2257:1182 (52.6:27.6)	2235:1150 (53.2:27.4)	22:32 (25.3:36.8)	<0.001	0.02
PSC cataract (no:yes; %)	2919:520 (68.1:12.1)	2878:507 (68.5:12.1)	41:13 (47.1:14.9)	0.08	0.37
Cortical cataract (no:yes; %)	2091:1348 (48.8:31.4)	2059:1326 (49.0:31.6)	32:22 (36.8:25.3)	0.88	0.28
Lens status (%)				<0.001	<0.001
Phakic	3439 (80.2)	3385 (80.6)	54 (62.1)		
Pseudophakic	711 (16.6)	686 (16.3)	25 (28.7)		
Aphakic	114 (2.7)	106 (2.5)	8 (9.2)		
BMI (%)				0.001	0.002
Normal	1977 (46.1)	1935 (46.1)	42 (48.3)		
Underweight	765 (17.8)	739 (17.6)	26 (29.9)		
Overweight	867 (20.2)	862 (20.5)	5 (5.7)		
Obese	283 (6.6)	279 (6.6)	4 (4.6)		
Manual-to-nonmanual occupation ratio (%)	2641:1647 (61.6:38.4)	2592:1609 (61.7:38.3)	49:38 (56.3:43.7)	0.32	0.31
Smoking (no:yes; %)	3419:869 (79.7:20.3)	3357:844 (79.9:20.1)	25:62 (28.7:71.3)	0.06	0.07
Smokeless tobacco use (no:yes; %)	3503:785 (81.7:18.3)	3442:759 (81.9:18.1)	26:61 (29.9:70.1)	0.007	0.02
Alcohol consumption (no:yes; %)	3412:876 (79.6:20.4)	3354:847 (79.8:20.2)	29:58 (33.3:66.7)	0.004	0.009
Literate-to-illiterate ratio (%)	1343:2945 (31.3:68.7)	1298:2903 (30.9:69.1)	45:42 (51.7:48.3)	<0.001	<0.001

BMI = body mass index; CCT = central corneal thickness; IOP = intraocular pressure; PSC = posterior subcapsular cataract.
*Mean ± standard deviation.

In this study, significant baseline risk factors that predicted incident pseudoexfoliation were older age, rural residence, illiteracy, nuclear cataract, and pseudophakia. Unlike the other studies on incident pseudoexfoliation,[31–33] we did not see an association of female gender with incident pseudoexfoliation. However, similar to other findings, we also found that incident pseudoexfoliation increased significantly with age. In comparison with the 50-to-59-year age group, the odds of pseudoexfoliation developing was almost 3 times higher for those 70 years of age or older. Because both pseudoexfoliation and cataract or cataract surgery are age-related conditions, they are likely to coexist. In view of this, our incident pseudoexfoliation estimate, where pseudophakics also were included, is probably more accurate for the population studied than that of the Iceland study.[31] In our study, there seem to be significant differences in incident pseudoexfoliation between rural and urban populations. In comparison with the urban population, the risk of incident pseudoexfoliation was 3 times more for the rural population. We noted a similar trend even in our prevalence study (unpublished data). The age- and gender-adjusted prevalence of pseudoexfoliation for our rural population was 4.74% (95% CI, 4.7–4.8) and that for our urban population was 2.05% (95% CI, 2.0–2.1). The effect of sunshine and pseudoexfoliation has been studied, and reports are conflicting. Some show that exposure to greater sunshine and lower ambient temperatures increase the likelihood of pseudoexfoliation,[38] whereas others did not show association.[39] In our study, people in rural areas are more likely to be outdoor workers, resulting in more exposure to sunshine and pseudoexfoliation. The significant association of illiteracy and incident pseudoexfoliation also is linked to this, because those who are illiterate are more likely to be outdoor manual workers and therefore are at a higher risk for incident pseudoexfoliation.

Nuclear cataract at baseline was a significant risk factor for incident pseudoexfoliation in our study population. In the past, prevalence studies from India and our prevalence data (Vijaya L, et al, unpublished data, 2015) for pseudoexfoliation have shown a similar association.[27,29] Cataract development may be linked to ocular ischemia, hypoxia, and reduced protection against ultraviolet rays resulting from lower levels of ascorbic acid in the aqueous humor.[1–3] Kanthan et al,[40] in a long-term follow-up study from the Blue Mountains Eye Study in subjects 49 years of age or older, reported a significant association ($P < 0.0001$) of incidence of nuclear cataract and cataract surgery in people with baseline pseudoexfoliation. Similarly, in a 12-year incidence study from Iceland, cataract surgery was found to be 3 to 4 times more likely in

Table 3. Baseline Risk Factors for Incident Pseudoexfoliation in the Chennai Eye Disease Study

Baseline Risk Factors	Study Population	Adjusted Odds Ratio (95% Confidence Interval)	P Value
Age (yrs)			
40–49	1907	1.00	<0.001
50–59	1233	4.7 (2.4–9.4)	<0.001
60–69	857	5.2 (2.5–10.7)	<0.001
70+	291	12.9 (6.1–27.2)	
Gender			
Male	1897	1.00	0.18
Female	2391	0.75 (0.48–1.2)	
Location			
Urban	1873	1.00	<0.001
Rural	2415	3.3 (1.9–5.5)	
Nuclear cataract			0.05
No	2914	1.00	
Yes	1027	1.85 (1.01–3.39)	
Lens status			
Phakic	3950	1.00	0.04
Pseudophakic	219	2.01 (1.1–3.9)	0.24
Aphakic	106	1.67 (0.7–3.9)	
Body mass index			
Normal	1977	1.00	0.67
Underweight	765	1.12 (0.66–1.89)	0.08
Overweight	867	0.42 (0.16–1.09)	0.68
Obese	283	1.26 (0.43–3.74)	
Smokeless tobacco use			
No	3503	1.00	0.62
Yes	785	0.89 (0.54–1.44)	
Alcohol consumption			
No	3412	1.00	0.10
Yes	876	0.62 (0.34–1.10)	
Literacy status			
Literate	1343	1.00	0.02
Illiterate	2945	1.79 (1.09–2.95)	

eyes with pseudoexfoliation than without.[33] We found higher rates ($P < 0.001$) of cataract surgery among those with pseudoexfoliation (37.9%) compared with those without pseudoexfoliation (18.9%). It does seem that eyes with pseudoexfoliation are at a higher risk of nuclear cataract developing or undergoing cataract surgery.

We found that the presence of pseudophakia at baseline was a significant risk factor for incident pseudoexfoliation.

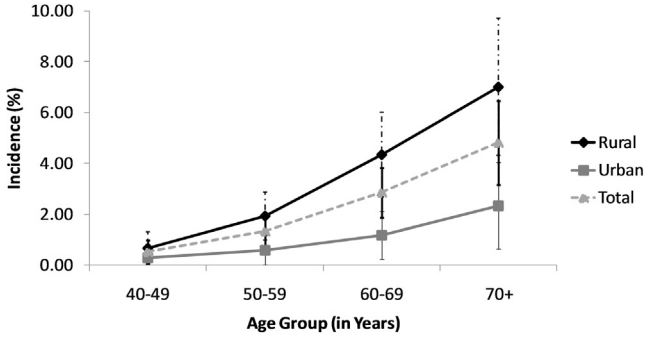


Figure 1. The association of age and incidence of pseudoexfoliation with 95% confidence intervals in the Chennai Eye Disease Incidence Study.

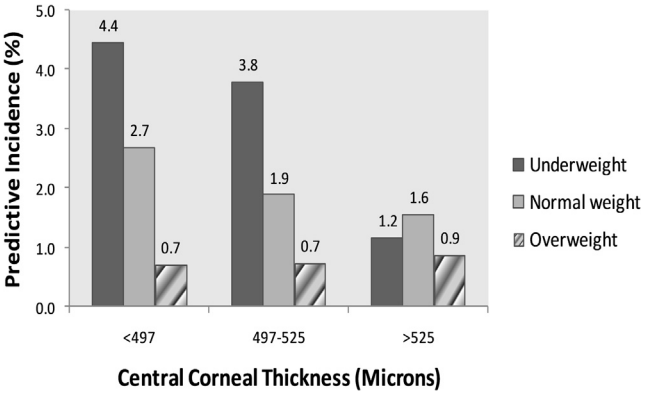


Figure 2. The relationship between stratified central corneal thickness and body mass index for incident pseudoexfoliation in the Chennai Eye Disease Incidence Study.

This can be explained in 2 ways. Cataract and pseudoexfoliation are age-related changes, and they can coexist or may precede one other. In this study, subjects with pseudoexfoliation may have had cataract first, and later pseudoexfoliation developed. It is also possible that the study subjects had some amount of pseudoexfoliation and that the pseudoexfoliation material might have been washed out in the course of the cataract surgery. During the follow-up period, it might have become redeposited. A large proportion (11.5%) of incident pseudoexfoliation subjects had PACS. It is clinically well known that pseudoexfoliation material deposits on the zonules causes zonular weakness. This can lead to an anterior shift of the lens and PACS.[3] This is substantially higher than the 2.6% incident PACS that we reported in this population.[41] Independently, CCT and BMI were not risk factors for pseudoexfoliation. However, incident pseudoexfoliation was more common in people with thinner corneas and lower BMI. At present, we are unable to provide a possible explanation for this association.

Any population-based longitudinal study will have its strengths and weaknesses. The major strength of this study is its large, population-based longitudinal design, with well-defined criteria, adherence to standardized protocols, and completeness of data collection. As in other population-based incident studies, the main weakness of the study is loss to follow-up. The main causes for loss to follow-up were inability to contact subjects, mortality, and migration. In comparison with participants, nonparticipants were older, and this could have influenced the magnitude of the pseudoexfoliation incidence rates. In this long-term study, we report the 6-year incidence of pseudoexfoliation and its associated baseline risk factors from a South Indian cohort. The available information about the incidence of pseudoexfoliation is very limited, and our results are a valuable addition.

References

1. Naumann GOH, Schlötzer-Schrehardt U, Küchle M. Pseudoexfoliation syndrome for the comprehensive ophthalmologist: intraocular and systemic manifestations. Ophthalmology 1998;105:951–68.

2. Ritch R, Schlötzer-Schrehardt U. Exfoliation syndrome. Surv Ophthalmol 2001;45:265–315.
3. Schlötzer-Schrehardt U, Naumann GOH. Ocular and systemic pseudoexfoliation syndrome. Am J Ophthalmol 2006;141: 921–37.
4. Ritch R. Exfoliation syndrome-the most common identifiable cause of open-angle glaucoma. J Glaucoma 1994;3:176–8.
5. Ritch R. Exfoliation syndrome and occludable angles. Trans Am Ophthlmol Soc 1994;92:845–944.
6. Gross FJ, Tingey D, Epstein DL. Increased prevalence of occludable angles and angle-closure glaucoma in patients with pseudoexfoliation. Am J Ophthalmol 1994;117:333–6.
7. Thorleifsson G, Magnusson KP, Sulem P, et al. Common sequence variants in the LOXL1 gene confer susceptibility to exfoliation glaucoma. Science 2007;317:1397–400.
8. Ramprasad VL, George R, Soumittra N, et al. Association of non-synonymous single nucleotide polymorphisms in the LOXL1 gene with pseudoexfoliation syndrome in India. Mol Vis 2008;14:318–22.
9. Nouri-Mahdavi K, Nosrat N, Sahebghalam R, Jahanmard M. Pseudoexfoliation syndrome in central Iran: a population-based survey. Acta Ophthalmol Scand 1999;77:581–4.
10. McCarty CA, Taylor HR. Pseudoexfoliation syndrome in Australian adults. Am J Ophthalmol 2000;129:629–33.
11. Mitchell P, Wang JJ, Hourihan F. The relationship between glaucoma and pseudoexfoliation: the Blue Mountains Eye Study. Arch Ophthalmol 1999;117:1319–24.
12. Rotchford AP, Kirwan JF, Johnson GJ, Roux P. Exfoliation syndrome in black South Africans. Arch Ophthalmol 2003;121:863–70.
13. Foster PJ, Seah SK. The prevalence of pseudoexfoliation syndrome in Chinese people: the Tanjong Pagar Survey. Br J Ophthalmol 2005;89:239–40.
14. Miyazaki M, Kubota T, Kubo M, et al. The prevalence of pseudoexfoliation syndrome in a Japanese population: the Hisayama study. J Glaucoma 2005;14:482–4.
15. Abdul-Rahman AM, Casson RJ, Newland HS, et al. Pseudoexfoliation in a rural Burmese population: the Meiktila Eye Study. Br J Ophthalmol 2008;92:1325–8.
16. Rudkin AK, Edussuriya K, Sennanayake S, et al. Prevalence of exfoliation syndrome in central Sri Lanka: the Kandy Eye Study. Br J Ophthalmol 2008;92:1595–8.
17. Viso E, Rodriguez-Ares MT, Gude F. Prevalence of pseudoexfoliation syndrome among adult Spanish in the Salnes eye Study. Ophthalmic Epidemiol 2010;17:118–24.
18. Kang JH, Loomis S, Wiggs JL, et al. Demographic and geographic features of exfoliation glaucoma in 2 United States-based prospective cohorts. Ophthalmology 2012;119: 27–35.
19. You QS, Xu L, Wang YX, et al. Pseudoexfoliation: normative data and associations: the Beijing eye study 2011. Ophthalmology 2013;120:1551–8.
20. Pakravan M, Yazdani S, Javadi MA, et al. A population-based survey of the prevalence and types of glaucoma in central Iran: Yazd eye study. Ophthalmology 2013;120:1977–84.
21. Forsman E, Cantor RM, Lu A, et al. Exfoliation syndrome: prevalence and inheritance in a sub isolate of the Finnish population. Acta Ophthalmol Scand 2007;85:500–7.
22. Arnarsson A, Damji KF, Sverrisson T, et al. Pseudoexfoliation in the Reykjavik Eye Study: prevalence and related ophthalmological variables. Acta Ophthalmol Scand 2007;85:822–7.
23. Aström S, Lindén C. Incidence and prevalence of pseudoexfoliation and open-angle glaucoma in northern Sweden: I. Baseline report. Acta Ophthalmol Scand 2007;85:828–31.
24. Anastasopoulos E, Topouzis F, Wilson MR, et al. Characteristics of pseudoexfoliation in the Thessaloniki Eye Study. J Glaucoma 2011;20:160–6.
25. Allingham RR, Loftsdottir M, Gottfredsdottir MS, et al. Pseudoexfoliation syndrome in Icelandic families. Br J Ophthalmol 2001;85:702–7.
26. Topouzis F, Wilson R, Harris A, et al. Prevalence of open-angle glaucoma in Greece: the Thessaloniki Eye Study. Am J Ophthalmol 2007;144:511–9.
27. Krishnadas R, Nirmalan PK, Ramakrishnan R, et al. Pseudoexfoliation in a rural population of southern India: the Aravind Comprehensive Eye Survey. Am J Ophthalmol 2003;135:830–7.
28. Arvind H, Raju P, Paul PG, et al. Pseudoexfoliation in South India. Br J Ophthalmol 2003;87:1321–3.
29. Thomas R, Nirmalan PK, Krishnaiah S. Pseudoexfoliation in southern India: the Andhra Pradesh Eye Disease Study. Invest Ophthalmol Vis Sci 2005;46:1170–6.
30. Jonas JB, Nangia V, Matin A, et al. Pseudoexfoliation: Normative Data and Associations. The Central India Eye and Medical Study. PLOS One 2013;8(10):e76770.
31. Arnarsson A, Damji KF, Sasaki H, et al. Pseudoexfoliation in the Reykjavik Eye Study: 5-year incidence and changes in related ophthalmological variables. Am J Ophthalmol 2009;148:291–7.
32. Karger RA, Jeng SM, Johnson DH, et al. Estimated incidence of pseudoexfoliation syndrome and pseudoexfoliation glaucoma in Olmsted County, Minnesota. J Glaucoma 2003;12: 193–7.
33. Arnarsson A, Sasaki H, Jonasson F. Twelve-year incidence of exfoliation syndrome in the Reykjavik Eye Study. Acta Ophthalmol 2013;91:157–62.
34. Arvind H, Paul PG, Raju P, et al. Methods and design of the Chennai Glaucoma Study. Ophthalmic Epidemiol 2003;10: 337–48.
35. Foster PJ, Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol 2002;86:238–42.
36. Vijaya L, George R, Paul PG, et al. Prevalence of open angle glaucoma in a rural South Indian population. Invest Ophthalmol Vis Sci 2005;46:4461–7.
37. Vijaya L, George R, Baskaran M, et al. Prevalence of primary open angle glaucoma in an urban South Indian population and comparison with a rural population. The Chennai Glaucoma Study. Ophthalmology 2008;115:648–54.
38. Stein JD, Pasquale LR, Talwar N, et al. Geographic and climatic factors associated with exfoliation syndrome. Arch Ophthalmol 2011;129:1053–60.
39. Arnarsson A, Jonasson F, Damji KF, et al. Exfoliation syndrome in the Reykjavik Eye Study: risk factors for baseline prevalence and 5-year incidence. Br J Ophthalmol 2010;94: 831–5.
40. Kanthan GL, Mitchell P, Burlutsky G, et al. Pseudoexfoliation syndrome and the long-term incidence of cataract and cataract surgery: the Blue Mountains Eye study. Am J Ophthalmol 2013;155:83–8.
41. Vijaya L, Asokan R, Panday M, et al. Six-year incidence of angle-closure disease in a South Indian population: the Chennai Eye Disease Incidence Study. Am J Ophthalmol 2013;156:1308–15.

Footnotes and Financial Disclosures

Originally received: September 22, 2014.
Final revision: January 21, 2015.
Accepted: February 5, 2015.
Available online: March 19, 2015. Manuscript no. 2014-1519.

[1] Glaucoma Project, Vision Research Foundation, Sankara Nethralaya, Chennai, India.

[2] Elite School of Optometry, Chennai, India.

[3] Birla Institute of Technology and Science, Pilani, India.

*Both Dr. Vijaya and Dr. George contributed equally as first authors.

Financial Disclosure(s):
The author(s) have no proprietary or commercial interest in any materials discussed in this article.

Supported by the Chennai Willingdon Corporate Foundation, Chennai, India.

Author Contributions:

Conception and design: Vijaya, Asokan, Panday, Choudhari, Ve Ramesh, Velumuri, George

Analysis and interpretation: Vijaya, Asokan, Panday, George

Data collection: Vijaya, Asokan, Panday, Choudhari, Ve Ramesh, Velumuri, George

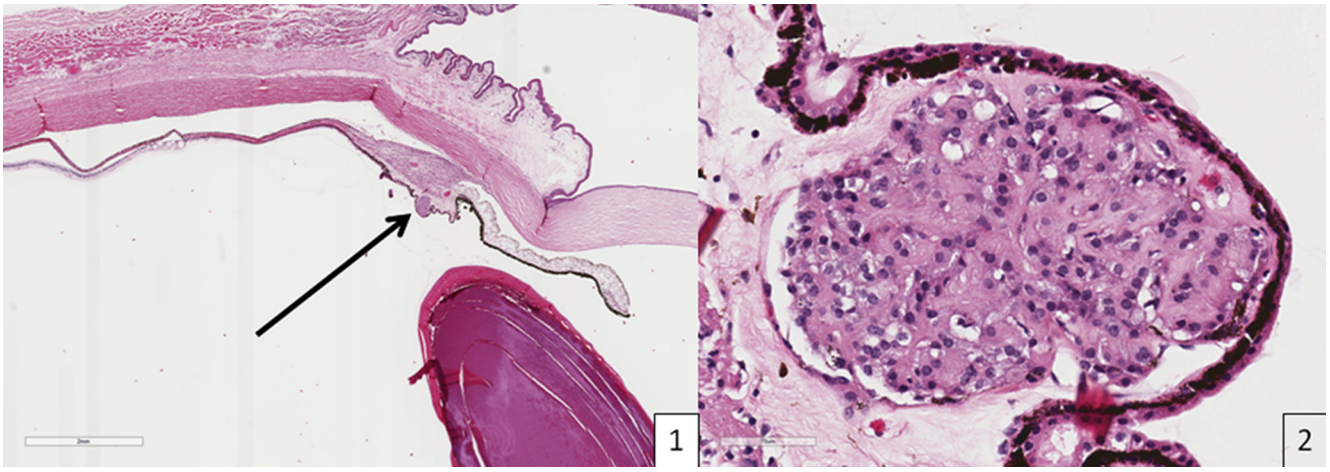
Obtained funding: Not applicable

Overall responsibility: Vijaya, Asokan, Panday, George

Abbreviations and Acronyms:
BMI = body mass index; **CDR** = cup-to-disc ratio; **CI** = confidence interval; **D** = diopter; **IOP** = intraocular pressure; **PACS** = primary angle-closure suspect.

Correspondence:
Lingam Vijaya, MS, Medical Research Foundation, Sankara Nethralaya, 18, College Road, Chennai, India 600 006. E-mail: cgscedis@gmail.com.

Pictures & Perspectives



Fuchs' Adenoma

Fuchs' adenoma in a 60-year-old man who underwent subtotal orbital exenteration for intraorbital spread of basal cell carcinoma. An adenomatous proliferation can be seen (arrow) on the nonpigmented ciliary epithelium with hematoxylin and eosin staining (Fig 1). The lesion consists of amorphous eosinophilic material and mucopolysaccharides (Fig 2). This lesion is benign and generally seen as an incidental finding in older adults.

Krishna R. Surapaneni, MD
Alexander L. Ringeisen, MD
Paul O. Phelps, MD

University of Wisconsin — Madison, Department of Ophthalmology and Visual Sciences, Madison, Wisconsin