ORIGINAL RESEARCH

Prevalence of Pseudoexfoliation Among Adults and Its Related Ophthalmic Variables in Southern Ethiopia: A Cross-Sectional Study

Ephrem Kibru Melese, Menen Ayalew Shibeshi, Sadik Taju Sherief 🆔

Department of Ophthalmology, School of Medicine, College of Health Sciences, Addis Ababa University, Addis Ababa, Ethiopia

Correspondence: Sadik Taju Sherief, Department of Ophthalmology, School of Medicine, College of Health Sciences, Addis Ababa University, P.O. Box 9086, Addis Ababa, Ethiopia, Email goge4000@yahoo.com

Purpose: A community-based study was conducted to determine the prevalence and sociodemographic factors of pseudoexfoliation syndrome among adults in Southern Ethiopia.

Patients and Methods: A community-based cross-sectional study was conducted among subjects aged 40 years or older. Subjects underwent standardized examination, including portable slit-lamp biomicroscopy before and after pupillary dilatation, and intraocular pressure measurement using Tono-Pen. Pseudoexfoliation was diagnosed on slit-lamp examination by the presence of white dandruff-like material on the pupillary margin and/or on the anterior lens capsule of one or both eyes.

Results: Among 760 participants, the prevalence of pseudoexfoliation was 12.0% (95% confidence interval: 9.7–14.3%). The mean age of pseudoexfoliation cases was 63.9 years (SD 9.96, age range 40–90 years). The prevalence increased with increasing age, with 26.9% of those 60 or older affected. Slightly higher proportion of males (12.4%) were found to have pseudoexfoliation in either of the eyes than females (11.6%) which was not statistically significant (p = 0.738). Mean IOP in subjects with pseudoexfoliation was found to be 20.65 ± 5.15 mmHg, while it was 15.0 ± 2.3 mmHg for those without pseudoexfoliation. The difference between the two populations was found to be statistically significant (P < 0.05).

Conclusion: The prevalence of pseudoexfoliation in eyes of people in Southern Ethiopia appears greater than that reported in other places of Africa and Asia. Pseudoexfoliation occurs at a relatively younger age in our population. Increasing age is associated with the presence of pseudoexfoliation, and pseudoexfoliation in turn is associated with higher intraocular pressure.

Keywords: pseudoexfoliation, intraocular pressure, glaucoma, rural community

Introduction

Pseudoexfoliation (PXF) is characterized by the accumulation of extracellular fibrillar material in many ocular and systemic tissues[1] and is often associated with glaucoma.[2]

PXF is an age-related syndrome with wide geographic variations in prevalence,[3–9] even within the same population.[7] The differences in prevalence have not been well explained. These variations may be either a true biological, ecological, or may even be differences related to examination techniques and diagnostic abilities.

A high prevalence of PXF in a developing country, with a large proportion of blindness due cataract and glaucoma is important for three reasons. The first is that PXF is associated with weak zonules and an increased risk for complications during cataract surgery,[10] secondly; a clinical observation of PXF may be used as a marker to identify an individual at risk of glaucoma. Finally, an association between PXF and angle-closure glaucoma[10,11] has been found in some ethnic groups and PXF may act as a marker to identify those with this form of glaucoma.

Clinical studies in hospital settings in Ethiopia using patients having ocular morbidities have shown high prevalence of PXF.[12,13]

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No population-based prevalence studies of PXF have been published from Ethiopia. A study in South Africa revealed a prevalence of 0.08% in adults over the age of 40.[14] It is unclear whether the general population in Ethiopia has a high prevalence of PXF.

This study aimed to determine the prevalence of PXF in a community in southern Ethiopia among adults of 40 years and older and identify its relationship to some ophthalmic variables.

Patients and Methods

This was a cross-sectional community-based study that was conducted in Kebena woreda of the Gurage Zone, Southern Nations and Nationalities of People (SNNP) region, Ethiopia, from January 2017 to February 2017. This district is located 155 kilometers from Addis Ababa and consisted of 23 kebeles. The total population of the area was 70,839 for the year 2017. There were estimated 14,000 households, and the mean household size was 5 people. The study population was residents of Kebena district who were 40 years and older.

Sample Size Calculation

Using a prevalence of 0.08 (taken from the population-based study in South Africa),[14] a margin of error of 2%, and a confidence limit of 95% and a non-response rate of 15%, a sample size of 784 were established.

Sampling Strategy

Sampling Technique

Multi-stage sampling with probability proportional to size was employed to select the sample. Kebeles were taken as first-stage sampling units. A kebele is the smallest administrative unit of Ethiopia. Each kebele consists of at least 500 families, or the equivalent of 3500 to 4000 persons. It is part of a woreda. The list of current kebeles in the woreda was obtained from the local administration and a random sample of 10 kebeles was taken from all the 23 kebeles in the woreda. Households in each of the selected kebeles served as second-stage units. A household constitutes a person or group of persons, irrespective of whether related or not, who normally live together in the same housing unit or group of housing units and who have common cooking arrangements. A systematic random sampling was used to select the sampling units. The total sample size calculated for the district was distributed for the kebeles based on their population size, sample allocation using probability proportional to size (PPS) technique. The sampling interval was subsequently calculated using the number of households in the 10 Kebeles divided by the required number of households (ie 6025/ 784=7) and the starting point (sampling unit) was determined using lottery method. Every seventh household was then eligible for inclusion.

One individual above the age of 40 was eligible for examination from each of the selected households, and a lottery method was used when there was more than one individual in the selected households.

Data Collection Method

Each eligible household was visited, and a study subject selected. Sociodemographic data were filled in the questionnaire, and visual acuity of both eyes separately was assessed outside the house in a shaded area. Visual acuity was measured using tumbling-E Snellen chart, and whenever the visual acuity was found to be worse than 6/9, a pin hole was used to account for possible refractive error. Both eyes of all subjects were examined using a portable slit lamp before and after pupillary dilatation for signs of PXF in the anterior segment. PXF was diagnosed on slit-lamp biomicroscopy by the presence of white dandruff-like material at the pupillary margin and/or on the anterior lens capsule of one or both eyes. Intraocular pressure (IOP) was measured using Tono-Pen (Medtronic Solan, XL) before pupillary dilation. In order to estimate the width of the chamber angle, Van-Herick method was used and when the drainage angle was judged to be not occludable (the distance between the anterior surface of the iris and the posterior surface of the cornea is more than one-fourth the corneal thickness), the pupils were dilated with 1% tropicamide and 2.5% phenylephrine hydrochloride to allow examination of the lens. World Health Organization (WHO) Simplified Cataract Grading System was utilized to document about the status of the lens.[15] Cataract was said to be present when nuclear, cortical, or posterior subcapsular standards were 2 and above. Subjects having corneal opacification dense enough to obscure visualization of the anterior

segment, evidence of active or past attack of anterior uveitis, or a history of intraocular surgery for cataract, glaucoma, or retinal detachment were excluded. Best village-based visual acuity was defined as the better of presenting and pinhole visual acuity, as measured during data collection. The definition of vision status was based on the WHO categories of visual impairment. Blindness was defined as a presenting VA of less than 3/60 in the better eye. Low vision was defined as presenting VA of at least 3/60 but less than 6/18 in the better eye. The term "monocular visual impairment", which is not a WHO classification, was used to describe participants who had low vision or blindness in one eye and normal or nearly normal vision in the other (both eyes had VAs of at least 6/18).[16]

The study and data collection were conducted in accordance with the principles of the Declaration of Helsinki. Informed verbal consent was approved by the research ethical committee of the School of Medicine, Addis Ababa University. Informed verbal consent was taken from all study participants.

Statistical Analysis

Data was entered into a computer and edited for any inconsistencies before analysis using SPSS for Windows Version 15.0 to calculate means, cross tabulations and X^2 tests. Odds ratios were used to assess the odds of having increased IOP with and without PXF. Associations between PXF, demographic factors, and, other ocular diseases were computed using either the X^2 or Fisher's exact test, and P-values below 0.05 were considered statistically significant. Odds ratios were calculated, separately for right and left eyes, to test for associations between PXF and IOP, and PXF and senile lens changes.

Results

A total of 760 subjects were examined, giving a response rate of 96.8%. Three hundred fifty-five (46.7%) were males and 405 (53.3%) were females. The mean age was 54 (SD 9.74) (range 40–90) years. Table 1 shows the age and sex distribution of the study subjects.

Of the total eligible population (760 subjects), 93 were found to have PXF in one or both eyes, a prevalence of 12.2% (95% CI: 9.7−14.3%). Of the 93 participants with PXF, 51 (56%) were found to have bilateral PXF (95% CI: 46−66%).

The mean age of participants with PXF was 63.9 years (SD 9.962, range 40–90 years), while it was 52.63 (SD 8.90, range 40–90 years) for those without PXF. The difference was found to be statistically significant (95% CI: 9.18–13.11%, P = 0.00).

Prevalence of PXF increased with age (X^2 test; P = 0.000) and was highest among subjects aged >70 years. Sixty-six (26.9%) subjects of 60 years or older had PXF in one or both eyes and 50% of the subjects above the age of 70 were found to have PXF. Age-specific prevalence rates are shown in Table 2.

Odds ratios for the likelihood of developing either unilateral or bilateral PXF syndrome, by age are also displayed in the table with the 40–50-year age group as reference. The older groups all had significantly higher ORs than the reference group.

Slightly higher proportion of males (12.4%) were found to have PXF in either of the eyes than females (11.6%) which was not statistically significant (p=0.738), even after standardization for age differences (p=0.317; age adjusted odds ratio, 1.29; 95% confidence interval: 0.79–2.11).

Table 1 Distribution of the Study Subjects by Age and Sex, Prevalence of PXF Among Adults in Kebena Woreda, Gurage Zone: January 2017

Age Range	Male n (% Column)	Men with PXF n (% Row)	Female n (% Column)	Women with PXF n (% Row)	Total No of Subjects Examined n (% Row)
40–49	98 (27.6)	1 (1.0)	94 (23.2)	1 (1.1)	192 (25.3)
50–59	127 (35.8)	8 (6.3)	196 (48.4)	15 (7.7)	323 (42.5)
60–69	86 (24.2)	12 (14.0)	95 (23.5)	23 (24.2)	181 (23.8)
70–79	38 (10.7)	21 (55.3)	18 (4.4)	6 (33.3)	56 (7.4)
80–90	6 (1.7)	2 (33.3)	2 (0.5)	2 (100.0)	8 (1.1)
Total	355 (100)	44 (12.4)	405 (100)	47 (11.6)	760 (100)

Table 2 Prevalence of PXF According to Age Among Adults in Kebena Woreda, Gurage Zone: January 2017

Age Range	No. Examined	Unilateral PXF n (% row)	PXF in OD & OS n (% Row)	PXF in One or Both Eyes, n (% row)	OR (95% CI) for PXF in One or Both Eyes	P-value
40–50	360	7 (1.9)	4 (1.1)	11 (3.1)	1.00	0.000
51–60	283	19 (6.7)	19 (6.7)	38 (13.4)	4.7 (3.7–9.7)	0.000
61–70	73	8 (11.0)	14 (19.2)	22 (30.1)	6.5 (3.3–12.8)	0.000
71–90	44	8 (18.2)	14 (31.8)	22 (50.0)	2.3 (1.1–5.1)	0.033
Total	760	42 (5.5)	51 (6.7)	93 (12.2)		

Features of PXF

In 68 eyes (47.2%), deposits were visible only at the pupillary border, while in 14 (9.7%) deposits could seen only on the anterior lens capsule. Deposits were present both at the pupillary border and on the anterior lens capsule in 62 eyes (43%).

Intraocular Pressure

The mean IOP of the right eye in the PXF population was 20.65 (SD 5.15) (range 12–45) mmHg and 15.0 (SD 2.30) (range 10–40) mmHg for the non-pseudoexfoliators. The mean difference of 5.65 mmHg between the two populations was found to be statistically significant (95% CI: 4.05–6.50 mmHg; p<0.0001).

The mean IOP of the left eye in the PXF population was 21.69 (SD 5.58) (range 12–39) mmHg and 15.50 (SD 1.90) (range 10–24) mmHg for the non-pseudoexfoliators. The mean difference of 6.19 mmHg between the two populations was statistically significant (95% CI: 4.88–7.51 mmHg; p<0.0001). The mean IOP of the eye with PXF in subjects with unilateral PXF was 19.45 (SD 3.78) mmHg, and bilateral PXF eyes had a mean IOP of 21.75 (SD 5.73) mmHg. But the mean difference of 1.70 mmHg between the two populations was not statistically significant (95% CI: 0.20–3.67 mmHg; p = 0.053). Fifty (34.7%) eyes with PXF syndrome had IOP higher than 21 mm Hg. And only 12 (0.8%) eyes without PXF were found to have IOP >21 mmHg (p < 0.001). Cataract was found in 59.2% of the eyes with PXF, but in only 13.5% of the non-PXF eyes (p < 0.001), indicating a strong association between cataract and PXF.

Table 3 presents data on the distribution between PXF and senile lens changes for right and left eye. In a univariate analysis, nuclear and posterior subcapsular cataract were found to be significantly associated with PXF (p=0.03). But when adjusted for age, the association becomes statistically insignificant.

Forty-eight (33.3%, 95% CI: 20.0–41.2) eyes with PXF had best village-based distance visual acuity of <6/60. The prevalence of low vision and blindness in the study population was 0.5% and 1.7%, respectively. But among subjects with PXF, 0.9% and 2.3% had blindness and low vision, respectively. The prevalence of impaired vision in the involved eye was significantly higher in subjects with PXF (age adjusted OR, 4.55; 95% CI: 2.26–9.18).

Discussion

This study confirms the high prevalence of PXF among the Kebena people in SNNPR, Ethiopia. The rate of 26.9% for those 60 or older in this study is even higher than highest published figures from Scandinavia, where the syndrome was

Table 3 The Association Distribution Between Pseudoexfoliation and Senile Lens Changes for Right and Left Eye Among Adults in Kebena Woreda, Gurage Zone: January 2017

Status of Lens	PXF in the Right Eye n (%)	PXF in the Left Eye n (%)
Clear	15 (30.8)	14 (19.4)
Nuclear cataract	8 (11.1)	10 (13.9)
Cortical cataract	18 (25.0)	20 (27.8)
Nuclear + PSC	16 (22.2)	12 (16.7)
Dense	15 (20.8)	16 (22.2)
Total	72 (100.0)	72 (100.0)

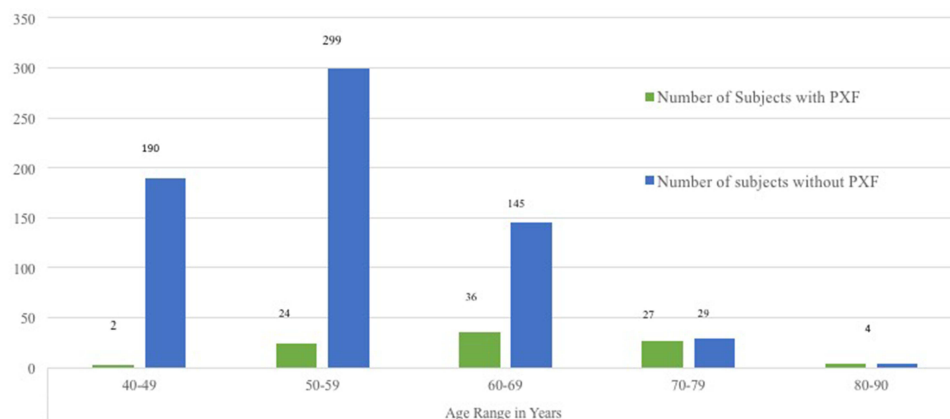**Table 4** The Prevalence of Pseudoexfoliation Across Population of Different Regions

Studies	Age (Years)	Sample Size	Location	Prevalence (%)
Forsius et al[7]	>50	99	Inuit Population	0
Cashwell et al[17]	30–94	2121	South Eastern USA	1.6
Hiller et al[19]	52–85	1999	Framingham population	1.8
Forsius et al[7]	>50	723	Peru	4.4
Forsius et al[7]	>50	382	Kökar, Aland, Finland	11
Melese et al (our)	>40	760	Ethiopia, Gurage	12
Forsius et al[7]	>50	208	Mariehamn, Aland, Finland	16.8
Forsius et al[7]	>50	219	Oulu Finland	22.4
Forsius et al[7]	>50	293	Reykjavík, Iceland	29

first reported. The reported prevalence rate of PXF syndrome in different populations shows extensive variations 0% in Eskimos,[7] 1.6% in a southeastern US population,[17] 1.8% in the Framingham Eye Study, 4.4–29% in the Scandinavian countries[7] (Table 4).

This finding therefore suggests both genetic and environmental influences even though differences in prevalence across populations need to be interpreted with caution considering the difficulties and lack of standardization in diagnosis and the potential for sub-clinical or early cases to be missed.

Two hospital-based published reports from Ethiopia described a high prevalence of PXF amongst patients with glaucoma or ocular hypertension (25.0%)[12] and cataract (39.3%).[13] However, this is the first population-based survey of the prevalence of PXF in Ethiopia. This study confirms the high prevalence of PXF in Ethiopia.

We found that the mean age of subjects with PEX syndrome is 11.27 years older than the normal population. Considering age-specific prevalence rates, there was a significant linear increase in prevalence with age (Figure 1). This is also in agreement with previous reports that have shown that the prevalence of PXF increases with advancing age.[4,8,18–23] One remarkable finding in our results is that PXF occurs at a relatively younger age in our population (mean age being 63.9 years; SD 9.96, range 40–90 years) compared to studies done in Iceland (mean age of 72)[23] and the Framingham study (mean age of 72.2).[18] This is also in agreement with findings in a hospital-based study in Ethiopia,[13] which has reported a mean age of 63.7 ± 10.7 years (range 47–91 years) in patients with PXF who were scheduled for cataract surgery. It has been suggested that persons living in lower latitudes appear to develop PXF at younger age.[24] Bartholomew reported a prevalence rate of 6.4% in the 30–39 years' age group among the Bantu of South Africa.[25] This

Figure 1 Distribution of PXF by age among adults in Kebena Woreda, Gurage Zone, Southern Ethiopia: January 2017.

finding could support the theory of genetic predisposition and environmental effects in the development of PXF even though the well-known difficulty of determining age in a largely illiterate community has to be acknowledged in our study.

There are conflicting reports of gender differences in the prevalence of PXF. Women were found to be more frequently affected than men in Reykjavik eye study of Iceland and the Framingham Eye Study. On the contrary, studies in Greece,[19] Iran,[22] and Turkey[26] have shown the reverse. We found the prevalence of PXF among men to be marginally higher than in women, but the difference was not statistically significant, which is in accordance with the findings of the South Indian study.[27]

The finding that a reasonable number of participants with PXF have clinically visible deposits only over the surface of the lens emphasizes the need for dilated lens examinations preoperatively.

Like many of the population-based studies,[19–21,28] we found IOP levels to be generally higher in eyes with PXF than in eyes without it. The mean IOP in subjects with PXF was 5.27 mmHg higher than in those without PXF which was significant.

High IOP (>21mmHg) was recorded in 36.1% of the subjects with PXF compared to 0.8% in subjects without PXF. The PXF population had a significantly increased prevalence of IOP over 21 mmHg. Although investigation for evidences of glaucoma is beyond the scope of this study, it seems that a significant number of subjects with PXF were found to have one of the major identified risk factor for glaucoma, ie, ocular hypertension.[29]

The increasing prevalence of PXF and cataract with age and the association of PXF with the most common type of cataract (nuclear and PSC cataract) have public health implications for our country. Improved healthcare results in a definite demographic shift toward aging that may result in a higher burden of both PXF and cataract. Eyes with PXF have a greater frequency of complications such as zonular dialysis, capsular rupture, and vitreous loss at the time of cataract extraction. The surgical procedure is more difficult because the pupil may not dilate well. It has also been shown that PXF patients have an increased risk of acute increase in IOP after cataract surgery.[30,31]

Postoperative complications of posterior capsular opacification; capsule contraction syndrome, intraocular lens decentration, and inflammation are also greater in eyes with PXF.

A preoperative diagnosis of PXF and appropriate precautions during surgery may help reduce the frequency of complications.

Recent studies from India[21] and Burma[22] have highlighted the association between PXF and visual morbidity rates. Similarly, in our study blindness was strongly associated with the presence of PXF in the univariate analysis. We found that 30.6% of those with PXF were blind, marginally higher than data reported in the Aravind Comprehensive Eye Study (ACES) from a different part of southern India (25.7%) and The Andhra Pradesh Eye Disease Study (20.5%).

Conclusion

Our study confirms that there is a high prevalence of PXF in our population associated with a relatively higher average IOP. With those findings, the following measures are recommended: IOP should routinely be measured objectively in every case of PXF as there is a high chance that ocular hypertension and glaucoma be associated with. Guidelines should also be developed about the special precautions that should be undertaken by cataract surgeons while managing patients with cataract with PXF. A high degree of suspicion should be maintained for the presence of PXF during routine ophthalmic examination, particularly in the elderly with high IOPs.

Further studies are recommended to scrutinize the reason why relatively younger adult are affected more frequently in our population and identify the cause of poor vision in patients with PXF, review the relationship between PXF and glaucoma in our population, further analyze the reason behind statistical difference high mean IOP in the right eye, and identify the conversion rate of unilateral PXF to bilateral PXF and development of ocular hypertension over a certain period of time.

Abbreviations

IOP, intraocular pressure; PPS, probability proportional to size; PXF, pseudoexfoliation; SNNP, Southern Nations and Nationalities of People; WHO, World Health Organization.

Data Sharing Statement

We will provide the data or will cooperate fully in obtaining and providing the data on which the manuscript is based for examination by the editors or their assignees; and I, as the corresponding author, agree to serve as the primary correspondent with the editorial office, to review the edited manuscript.

Ethical Approval and Consent to Participate

The study and data collection were conducted in accordance with the principles of the Declaration of Helsinki. Informed verbal consent was approved by the research ethical committee of the School of Medicine, Addis Ababa University. Informed verbal consent was taken from all study participants.

Consent for Publication

The manuscript represents original and valid work and that neither this manuscript nor one with substantially similar content under our authorship has been published or is being considered for publication elsewhere, except as described in the journal's submission form and cover letter submitted with the manuscript, and copies of closely related manuscripts have been provided. We agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved and if requested. All identifying information of subjects involved in the study has been appropriately anonymized.

Disclosure

The authors report no conflicts of interest in relation to this work.

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