AFRICAN JOURNAL OF HEALTH SCIENCES AND MEDICINE
AJHSM (2024)03:01
http://www.du.edu.et/duj

RESEARCH ARTICLE

Prevalence of Pseudoexfoliation Syndrome and Related Ocular Manifestations in Patients Scheduled for Cataract Surgery

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Received: 12 February 2023

Accepted: 13 June 2024

Published: 25 June 2024

DOI:10.20372/ajhsm.v03i01.02

Suggested Citation: Ayalew MA., Abrra AS., & Desta KA. Prevalence of Pseudoexfoliation Syndrome and Related Ocular Manifestations in Patients Scheduled for Cataract Surgery. Afri. J. Heal. Sci. Med; 2024, 03(01).

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Abstract

Background: Pseudoexfoliation syndrome is an age-related condition marked by the deposition of a distinct fibrillar extracellular material in the eyes and other organs. Affecting nearly 70 million people worldwide, it is linked to various ocular conditions and complications that can impact long-term visual outcomes.

Purpose: To determine the prevalence of pseudoexfoliation syndrome and ocular manifestations related to it among patients who were scheduled for cataract surgery.

Methods and material: A hospital-based cross-sectional study was conducted on consecutive 222 patients aged $\geq$ 40 years who were scheduled for cataract surgery. A structured questionnaire and an abstraction formant for ocular examination were used to collect data. The collected data were coded and entered into SPSS version 25 for analysis. Both descriptive and inferential statistical analyses were performed to present the results.

Results: The prevalence of pseudoexfoliation syndrome was 38.7% (86/222) (95% CI, 32.3– 45.5). In comparison to patients without pseudoexfoliation, patient with pseudoexfoliation had a higher mean age (67.7 $\pm$ 11.2 vs. 61.2 $\pm$ 10.1: P$<$ 0.001). Significant association were found with working conditions (P$<$ 0.001) and sex (P = 0.008), with outdoor workers and males being more affected. The mean intraocular pressure was higher in eyes with pseudoexfoliation (17.16 $\pm$ 3.83 vs. 15.63 $\pm$ 2.96$mmHg$: P = 0.001) and mean pupillary diameter after dilation was smaller (5.72 $\pm$ 0.86 vs. 6.73 $\pm$ 0.9 mm: P$<$0.001). All 24 eyes with phacodonesis or subluxation had pseudoexfoliation syndrome (P$<$ 0.001).

Conclusion and Recommendation: This study revealed a high prevalence of pseudoexfoliation syndrome (38.7%) among cataract patients. The condition was significantly associated with older age, working outdoors, male sex, higher intraocular pressure, poor pupillary dilation, and the presence of phacodonesis or subluxated lenses. Population-based studies are recommended to evaluate the prevalence of pseudoexfoliation in the general population, and further studies on cataract surgical outcomes in patients with pseudoexfoliation are recommended.

Keywords: Cataract, Hawassa, Ethiopia, Pseudoexfoliation syndrome

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1 Background

Pseudoexfoliation syndrome (PEX) is an age-related disease in which abnormal fibrillar extracellular material is produced and deposited nearly in all structures of the anterior segment, as well as in conjunctiva and orbital structures [1]. Lindberg was the first to describe this syndrome in 1917 [2].

Up to 30% of the population over 60 years of age and approximately 60–70 million people globally are affected by PEX. Its prevalence varies significantly by region and ethnicity, with rates ranging from 0% among Eskimos to 40.6% in Nordic individuals over 80. In people over 60, PEX prevalence is 25% in Iceland, 20% in Finland, 4% in England, and 0% among Inuit. Additionally, the disease seems to affect some ethnic groups and geographical areas within nations more frequently than others. Ethnic and intraregional variations are exemplified by US prevalence estimates of 1.6% in southeastern habitats compared with 38% in Navajo Indians [3].

Although several epidemiological studies on PEX have been conducted worldwide, there are few prevalence studies in the African context, and the burden of PEX on the continent is not well understood. According to one review article (2014) on PEX in sub-Saharan Africa, there was variation in the prevalence of PEX, ranging from 5.1% to 7.7% among patients aged 40 and above in population-based studies, while clinical-based studies showed even much wider variation [4]. Clinical-based research in Egypt and Somalia has revealed that the prevalence of PEX varies greatly, with respective rates of 4.14% and 40.9%‘ [6, 6]. In Ethiopia, there are a few clinical studies conducted to evaluate the prevalence of pseudoexfoliation. A study conducted at Menelik II and Jimma Hospitals, showed the prevalence of PEX was 39.3% and 35.82%, respectively[7,8].

PEX has several ocular impacts, notably its association with cataract development. This was demonstrated in findings where the patient with only one eye affected by PEX, cataract almost always begins in that same eye [9,10]. PEX is also a leading cause of glaucoma worldwide, contributing significantly to cases in certain countries. At Menelik Hospital, pseudoexfoliation glaucoma (PEXG) was the second most common glaucoma subtype (26.6%), following primary open-angle glaucoma (POAG) (37.7%) [11]. Additionally, PEX increase the risk of postoperative complications, including fibrinoid reaction, posterior synechiae, decentration or dislocation of the lens implant, and anterior capsule contraction. It also raises likelihood of intraoperative problems such as poorly dilated pupils, zonular weakness, and capsular break [12].

As mentioned, PEX is associated with various ocular conditions and complications that affect long-term visual outcomes. Given Ethiopia's diverse population with varying ethnic groups and geographical areas, assessing the prevalence of PEX and its ocular manifestation among cataract patients in southern Ethiopia, an area previously unexplored in this context, is crucial. This study aims to determine the prevalence of PEX and related ocular manifestations among patients scheduled for cataract surgery at the Hawassa University Comprehensive Hospital (HUCSH).

2 Material and methods

The study was a hospital-based cross-sectional study conducted from April 14 to October 14, 2022, in Hawassa University tertiary eye care center, which is located in Hawassa City, about 272 km away from the capital city of Ethiopia. The center was established in 2005 G.C and served over 12 million people from Sidama and its neighboring regions. The study was conducted on consecutive cataract patients aged $\geq$ 40 years who were admitted for cataract surgery at the HUCSH during the study period. Eyes with cataract related to trauma or previous ocular inflammation were excluded from the study.

Data were collected by senior ophthalmology residents who scheduled patients for surgery, with all ocular examination findings were completed after evaluating the patients together with the supervising ophthalmologist. A structured questionnaire and abstraction format for ocular examination were used for data collection. Visual acuity tested at 6 meters using the ‘Snellen E

chart' by trained nurses. The IOP was measured using a Schiotz tonometer (Riester Schiotz Tonometer, Germany), and all eyes were examined with a slit-lamp biomicroscope (Keeler, USA) before and after mydriasis. In a patient with bilateral cataract, the eye scheduled for the first surgery was included in the study. The fellow eyes of all patients were examined to determine the bilaterality of PEX and to select patients for postoperative fundus examination of the scheduled eye.

The presence of PEX was confirmed by looking for typical white, fluffy, or granular material at the pupillary margin or on the anterior lens capsule. Even subtle signs of fibrillar deposition were sufficient to diagnose PEX. ACD was assessed using the Van Herrick grading method; patients with grade II or less underwent gonioscopic examination with Goldman indirect goniolens. Tropicamide 1% eye drops administered twice at 5-minute intervals, and pupil assessed for maximum dilation after 15 – 20 min. Pupillary dilation was measured with a pupil gauge chart or penlight. Patients with abnormal pupillary reflex or relative afferent defect were excluded from the study of pupillary size. Poor pupillary dilatation was defined as a maximally dilated pupil size less than 6 mm.

Dilated examination of the optic nerve head (ONH) was performed preoperatively in both eyes whenever the ocular media allowed for examination of the posterior segment of the eye. In patients with IOP $>21mmHg$ in either eye or vertical cup-to-disc ratio (VCDR) greater than 0.6 in the fellow eye, ONH examination of the scheduled cataractous eye was done after surgery. Fundus examination was performed using a 90-diopter posterior pole lens (Volk, USA) and a slit lamp biomicroscope. A visual field test (VFT) was done for patients with suspicious optic nerve VCDR ratio between 0.6 – 0.85 in the scheduled eye. Glaucoma was diagnosed in eyes with VCDR ≥ 0.6 or asymmetry of VCDR ≥ 0.2 with a definite visual field defect consistent with glaucoma, or eyes with VCDR ≥ 0.85 without visual field testing, or those with evidence of previous glaucoma surgery or treatment. Cataract morphology was classified as mainly nuclear, cortical, posterior subscapular, and mixed cataract using a slit-lamp biomicroscope.

Data were coded, checked, and entered manually into the Statistical Package for Social Sciences (SPSS) version 25. All analyses were performed using the same statistical software. Categorical variables are summarized as frequencies and percentages, whereas normally distributed continuous variables are presented as means and standard deviations using descriptive statistics. Bivariate analysis was performed using the Pearson chi-square test and Student's t-test to determine the possible association between pseudoexfoliation and the study variables. Statistical significance was set at P-value <0.05.

3 Results

A total of 222 eyes from 222 patients admitted for cataract surgery at HUCSH during the study period were included. The minimum and maximum ages of the study participants were 40 and 90 years, respectively, with a mean age of 63.59 $\pm$ 10.98 years. Males made up 56.3% of the study participants, with a male to female ratio of 1.3:1. Majority of study participants resided in Sidama region (60.4%), and most of them were either farmers (55.9%) or housewives (24.8%). Nearly 58% of the study subjects worked outdoors (See table 1).

Pseudoexfoliation syndrome was diagnosed in 86 eyes (38.7%) out of the 222 eyes included in the study (95% CI, 32.3– 45.5). Pseudoexfoliation material deposits were observed at pupillary border in 54 (62.8%) of eyes with PEX, over the lens capsule in 7 (8.1%) eyes, and at both the pupillary border and lens capsule in 25(29.1%) of eyes. Regarding laterality, 69 (80.2%) had PEX bilaterally whereas 17 (19.8%) exclusively had it in the study eye. Three patients had a history of enucleation in the fellow eye; however, none of them had PEX in the study eye.

Table 1 Sociodemographic characteristics of patients admitted for cataract surgery at Hawassa University comprehensive Specialized Hospital, Hawassa, 2022(N=222)

Characteristics		Frequency (n)	Percentage (%)
Sex	Male	125	56.3
	Female	97	43.7
Age	40-50	31	14
	51-60	76	34.2
	61-70	71	32
	>70	44	19.8
Ethnicity	Sidama	104	46.8
	Oromo	66	29.7
	Amhara	19	8.6
	Kembata	11	5
	Wolayita	6	2.7
	Other	16	7.2
Residence	Sidama	134	60.4
	Oromia	70	31.5
	SNNP	18	8.1
Occupation	Farmer	124	55.9
	Housewife	55	24.8
	Civil servant	24	10.8
	Merchant	15	6.8
	Other	4	1.8
Workplace	Outdoor	12	8 57.7
	Indoor	94	42.3

Glaucoma was diagnosed in 15 eyes (6.8%), with 13 cases PEX glaucoma and 2 cases of POAG. None of the eyes included in the study had an ACD of $\leq +2$ using the Van Herrick technique. In 75% surgical treated eyes, the preoperative maximally dilated pupillary diameter was adequate. One patient with PEXG and relative afferent pupillary defect observed over the scheduled eye was excluded from the study of pupillary size after dilation. A mixed type of cataract morphology was observed in 74.3 % of the eyes, followed by posterior subscapular cataract (PSC) (22.5%). Phacodenosis/subluxation of cataractous lens were found in 24 (11%) eyes out of 222 studied (See table 2).

According to this study, the prevalence of PEX increased considerably with age, rising from 25.8% in the 5^{th} decade of life to 59% in individuals over 70 years ($P < 0.001$). The mean age of patients with PEX was 67.7 $\pm$ 11.2 years, while that of those without PEX was 61.2 $\pm$ 10.1 years. Statistical analysis revealed that the difference was statistically significant ($P< 0.001$). Male patients had a two-fold higher likelihood of having PEX than female patients (COR: 2.13, 95% CI; 1.2 – 3.74).

The study also showed 52.3% of study participants working outdoors had PEX, compared with only 20.2% of those working indoors. This difference was statistically significant ($P< 0.001$) (See table 3).

Table 2 Ocular findings of eyes scheduled for surgery among patients admitted for cataract surgery at Hawassa University comprehensive Specialized Hospital, Hawassa, 2022 (N=222)

Variable		Frequency, n	Percentage, %
Scheduled eye	OD	120	54.1
	OS	102	45.9
Preoperative uncorrected visual acuity	CF < 1m or LP	151	68
	CF @1m up to CF < @3m	51	23
	CF @3m up to < 6/60	16	7.2
	<6/18 up to 6/60	4	1.8
Preoperative IOP, $mmHg$	≤ 21	205	92.3
	> 21	17	7.7
Type of glaucoma	PEX glaucoma	13	5.9
	POAG	2	0.9
	Glaucoma suspect	4	1.8
	Ocular hypertension	2	0.9
Preoperative maximally dilated pupillary diameter*	Adequately dilated	166	75.1
	Poorly dilated	55	24.9
Cataract morphology	Mixed	165	74.3
	Posterior subcapsular	50	22.5
	Nuclear	6	2.7
	Cortical	1	0.5
Stability of lens	Stable	198	89.2
	Phacodonesis	23	10.4
	Subluxated	1	0.5

Preoperative maximally dilated pupillary diameter *N=221

Table 3 Relationship of Socio-demographic variables with ocular pseudoexfoliation syndrome among study participants admitted for cataract surgery at Hawassa University comprehensive Specialized Hospital, Hawassa, 2022

Independent variables		Presence of PEX		P value+	COR
		Yes n (%)	No n (%)		
Age	40-50	8 (25.8)	23 (74.2)	< 0.001	
	51-60	18 (23.7)	58 (76.3)		
	61-70	34 (47.9)	37 (52.1)		
	>70	26 (59.1)	18 (40.9)		4.15 (95% CI; 1.5 – 11.37)
Mean age		67.7±11.2	61.2±10.1	< 0.001*	
Sex	Male	58 (46.4)	67 (53.6)	0.008	2.13 (95% CI; 1.2 – 3.74)
	Female	28 (28.9)	69 (71.1)		
Ethnicity	Sidama	47 (45.2)	57 (54.8)	0.065	
	Oromo	25 (37.9)	41 (62.1)		
	Amhara	5 (26.3)	14 (73.7)		
	Kembata	1 (9.1)	10 (90.9)		
	Wolayita	4 (66.7)	2 (33.3)		
	Other	4 (25.0)	12 (75.0)		
Residence	Sidama	54 (40.3)	80 (59.7)	0.132	
	Oromia	29 (41.4)	41 (58.6)		
	SNNP	3 (16.7)	15 (83.3)		
	Other	1 (25.0)	3 (75.0)		
Workplace	Outdoor	67 (52.3)	61 (47.7)	<0.001	4.34(95% CI; 2.35 – 7.99)
	Indoor	19 (20.2)	75 (79.8)		

+Pearson's chi-square test, *Student's t-test, and COR – crude odds ratio

Compared to eyes without PEX, those with PEX had a significantly higher mean IOP (17.16 ± 3.83 $mmHg$ vs. 15.63 ± 2.96 $mmHg$; P = 0.001). Furthermore, 15.1% of patients with PEX had glaucoma compared to 1.5% of patients without PEX, and 17.4% of patients with PEX had an IOP >21 $mmHg$. These differences between the two groups were statistically significant (P < 0.001). The mean pupillary diameter after dilation in eyes with PEX (5.72 ± 0.86 $mmHg$) was significantly smaller than that in eyes without PEX (6.73 ± 0.9 $mmHg$) (P < 0.001) (See table 4).

Table 4 Intraocular pressure, presence of glaucoma, and fully dilated pupillary size comparison between eyes with and without PEX among patients admitted for cataract surgery at Hawassa University Comprehensive and Specialized Hospital, Hawassa, 2022

Variables		Presence of pseudoexfoliation		Bivariate analysis
		Yes n (%)	No n (%)	P value+
IOP, $mmHg$	> 21	15(17.4)	2(1.5)	< 0.001
	≤ 21	71(82.6)	134(98.5)	
Mean IOP, $mmHg$		17.16±3.83	15.63±2.96	0.001*
Glaucoma	Yes	13(15.1)	2(1.5)	< 0.001
	No	73(84.9)	134(98.5)	
Preoperative maximally dilated pupillary diameter, mm#	< 6	43(50)	12(8.8)	< 0.001
	≥ 6	43(50)	124(91.2)	
Mean fully dilated pupillary diameter, mm		5.72±0.86	6.73±0.9	<0.001*

+ Pearson chi-square test, * Student's t-test, # preoperative dilated pupillary diameter=221

All 24 eyes with phacodonesis or subluxation included in the study had PEX, whereas none of the eyes without PEX had such findings. This difference was statistically significant (P< 0.001) (See table 5).

Table 5 Preoperative uncorrected visual acuity and characteristic of cataract comparison between eyes with and without pseudoexfoliation among patients admitted for cataract surgery at Hawassa University Comprehensive and Specialized Hospital, Hawassa, 2022

Variables		Presence of pseudoexfoliation		Bivariate analysis
		Yes n (%)	No n (%)	P-value+
Cataract morphology	Mixed	66 (76.7)	99 (72.8)	0.807
	PSC	18 (20.9)	32 (23.5)	
	Nuclear	2 (2.3)	4 (2.9)	
	Cortical	0	1 (0.7)	
Lens stability	Stable	62 (72.1)	136 (100)	< 0.001
	Phacodonesis	23 (26.7)	0	
	Subluxated	1 (1.2)	0	
Preoperative uncorrected VA	CF < 1m or LP	65 (75.6)	86 (63.2)	0.268
	CF @1m up to CF < @3m	16 (18.6)	35 (25.7)	
	CF @3m up to < 6/60	4 (4.7)	12 (8.8)	
	<6/18 up to 6/60	1 (1.2)	3 (2.2)	

+ Pearson chi-square test, PSC - posterior subcapsular cataract

4 Discussions

In this study, the prevalence of PEX was 38.7% (95% CI, 32.3– 45.5) among patients with cataract. This prevalence is consistent with studies from other parts of Ethiopia such as Menelik Hospital, which reported 39.3% prevalence, and studies from Jimma and Gonder, which reported 35.82% and 35% prevalence respectively [7,8,13]. A comparable result was also observed in Somalia (40.9%), where the prevalence of PEX was studied in cataract patients scheduled for surgery [5]. These similarities in prevalence rates might be due to a similar study setting. However, prevalence in this study was higher than similar hospital-based studies conducted in Finland (25%), Serbia (17.5%), Spain (21.6%), India (22.1%), Jordan (10.3%), Turkey (16.4%), and Nigeria (2.7%) [4,12,14-18]. These observed disparities in prevalence could be explained by ethnic/racial and environmental factors. Additionally, a community-based study conducted in Baso and Worena District, central Ethiopia found the prevalence of PEX to be 13.2% among individuals ≥40 years old (90/682), which is significantly lower than the present study [19]. This discrepancy may be explained by a pattern documented in numerous studies, which shows the prevalence of PEX increases as study population shifts from the general population to hospital settings.

Our study showed that the proportion of patients with PEX significantly increased with age, with the mean age of the PEX group was significantly higher than that of the non-PEX group (67.7 vs. 61.2 years). This finding aligns with studies done in Menelik hospital (63.7 vs. 60.3 years) and Gonder (66.2 vs. 60.1) [7,13]. Studies done in Serbia (79.4 vs. 73.5), Turkey (74.4 vs. 69.3), and Somalia (71.3 vs. 64.7) also showed a similar trend. The correlation between increasing age and higher prevalence of PEX may be attributed to long-term environmental exposure, decline in cellular function with age, and deposition of exfoliative material over time [5,12,20].

Additionally, this study demonstrated that working outdoors increased the likelihood of developing PEX. This finding is in accordance with that of a study conducted in Gonder, Northern Ethiopia [13]. The fact that workplace conditions, not ethnicity, were significantly associated with the presence of PEX in this study may favor the findings of a study conducted in the USA that showed ambient temperature and sun exposure as more important environmental triggers of PEX than hereditary risk factors. This could be due to ultraviolet radiation up regulation of Lysyl oxidase homolog 1 (LOXL 1) gene expression, as well as elastic fiber proteins found in the exfoliation material [3,21].

Despite many studies showing no sex predilection or conflicting results regarding sex predilection in patients with PEX, our studies have shown proportion of males (46.4%) with PEX was higher than the proportion of females (28.9%) with PEX ($P = 0.008$) [7,9]. Similar male predilection was observed in studies conducted in Gonder, Ethiopia, and Nigeria [4,13]. Male preference for PEX in our study may be explained by the fact that more men than women (73.4% vs. 26.6%) employed in outdoor working conditions.

In this study, the incidence of glaucoma was significantly higher in eyes with PEX than without PEX (15.11% vs. 1.5%) ($P < 0.001$). Similar results were reported in other studies: 13.3% in Menelik Hospital (13.3% vs. 8.5%), 71% in Somalia (71% vs. 10.8%), 8.3% in Turkey (8.3% vs. 2.5%), and 17.4% in Spain (17.4% vs. 9.4%) [5,7,17,20]. Furthermore, the mean IOP in a patient with PEX was significantly higher than patients without PEX (17.16 ± 3.83 vs. 15.63 ± 2.96, $P = 0.001$). This result is consistent with previous studies [7,17]. Although the exact mechanism of IOP elevation in PEX is debatable, increased outflow resistance in the trabecular meshwork is the most widely accepted hypothesis [3].

The primary risk factors for intraoperative complications during cataract surgery in eyes with PEX are poor pupillary dilation and preoperative phacodonesis or lens subluxation related to zonular weakness [3]. In this study, the mean pupillary size after dilation in eyes with PEX was significantly lower than in eyes without PEX

(5.72 ± 0.86 vs. 6.73 ± 0.9) (P< 0.001). The difference in the proportion of patients with poor pupillary dilation between eyes with and without PEX was also statistically significant (50% vs. 8.8%) (P< 0.001). Similar results were observed in India, where mean pupillary dilation was 5.1 (±1.4) mm in PEX patients compared to 7.2 (±1.6) mm in non PEX patients (P = 0.03) [14]. Furthermore, all 24 eyes included in the study with phacodonesis and subluxation had PEX (P< 0.001). Infiltration of exfoliative material into the iris stroma can create a mechanical barrier to mydriasis, resulting in poor pupillary dilation. This can lead to smaller capsulorhexis, leaving weakened zonules more vulnerable to the traumatic forces of intraocular manipulation [22].

Since the study was restricted to cataract patients scheduled for surgery, it does not provide insights into the prevalence of PEX in the general population. Additionally, the cross-sectional design of the study prevents establishing a cause-and-effect relationship between the variables.

5 Conclusion

A high prevalence of PEX (38.7%) among patients with cataract was seen in the present study. PEX incidence increased with age, was more common in patients working outdoors, and was more frequent in males. The study also showed significantly higher mean IOP and glaucoma rates in eyes with PEX compared to those without. Preoperative conditions such as poor pupillary dilatation, phacodonesis or subluxation were notably more prevalent in PEX cases, suggesting a higher probability of intraoperative complications. To better understand PEX prevalence and its link to cataract, population-based studies are recommended. Healthcare policymakers should raise awareness of PEX and the related ocular conditions. Moreover, cataract patients with PEX should be properly evaluated preoperatively, and patients should be informed about possible surgical complications. Surgeons are recommended to be prepared to encounter potential intraoperative complications associated with PEX. Further studies on cataract surgical outcomes in patients with pseudoexfoliation are recommended.

Disclosure

The authors declare that they have no conflicts of interest to disclose.

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