

PSEUDOEXFOLIATION SYNDROME: PREVALENCE AND ITS ASSOCIATION WITH SOME PARAMETERS

متلازمة التقشر الكاذب: انتشارها وعلاقتها مع بعض المشعرات

Zuhair Al Jaffal, MD; Ammar Kayyali, MD (CIS)

د. زهير الجفّال، د. عمار كيالي

ملخص البحث

هدف البحث: تعتبر متلازمة التقشر الكاذب عامل خطورة معروفاً لتطور الساد والزرق وخلع العدسة. كما تترافق هذه المتلازمة مع زيادة احتمالية الاختلاطات خلال جراحة الساد بسبب ضعف التوسع الحدقي وضعف ألياف النطيفة العدسية. تهدف هذه الدراسة إلى تحديد شيوع متلازمة التقشر الكاذب عند المرضى المراجعين للعيادة العينية في مستشفى حلب الجامعي.

طرق البحث: تمت هذه الدراسة المستقبلية في الفترة الممتدة بين أيلول 2014 وحزيران 2015، حيث تم فحص 500 مريضاً تتجاوز أعمارهم الـ 40 عاماً من مراجعي العيادة العينية في مستشفى حلب الجامعي في أيام منفصلة من قبل نفس الطبيب. تم إجراء فحص مفصل لكل المرضى يتضمن القصة السريرية والعينية والفحص على جهاز المصباح الشقي وقياس الضغط داخل المقلة وتنظير زاوية البيت الأمامي وتنظير قعر العين بعد توسيع الحدقة. صنف المرضى الذين لديهم مواد قشرية دقيقة على المحفظة الأمامية للعدسة و/ أو حافة الحدقة في إحدى العينين أو كليهما كمصابين بمتلازمة التقشر الكاذب.

النتائج: شُخصت المتلازمة عند 8 مرضى من أصل 500 مريضاً مضمّنين في الدراسة (1.6%). كما شُخصت المتلازمة في 10 عيون من أصل 870 عيناً تم فحصها (1.14%). كان الشيوع المصحح بالنسبة للعمر لمتلازمة التقشر الكاذب عند المرضى بعمر أكثر أو يساوي 40 عاماً 0.97% (بفواصل ثقة 95%: 0.28-1.67) عندما حسب باستخدام الجهرة السورية كميّار؛ وكان الشيوع المصحح للعمر لمتلازمة التقشر الكاذب بعمر أكثر أو يساوي 40 عاماً 1.34% (بفواصل ثقة 95%: 0.38-2.30) عندما حسب باستخدام الجهرة العالمية لمنظمة الصحة العالمية WHO. بلغ متوسط العمر للمرضى المصابين بمتلازمة التقشر الكاذب 71.50 سنة (بانحراف معياري 7.91 والمدى 58-83). كانت متلازمة التقشر الكاذب ثنائية الجانب في 25% من الحالات. لوحظ ترافق هام لمتلازمة التقشر الكاذب مع الساد والزرق ونقص السمع. حيث لوحظ الساد عند 87.5% والزرق عند 37.5% ونقص السمع عند 37.5% من المصابين بالمتلازمة.

الاستنتاجات: تعتبر متلازمة التقشر الكاذب مرضاً مهماً عند المرضى كبار السن في سوريا كونها تترافق بزيادة حدوث الساد والزرق ونقص السمع.

ABSTRACT

Objective: Pseudoexfoliation (PXF) is a recognized risk factor for developing cataract, glaucoma and lens dislocation. PXF is also associated with increased risk of complications during cataract surgery due to poor mydriasis and zonular weakness. The aim of this study

is to report the prevalence of pseudoexfoliation among Syrians attending the ophthalmology clinic of Aleppo University Hospital.

Methods: A prospective study conducted in the period from September 2014 to June 2015. A total of 500 patients aged 40 years or older attending the general ophthalmic clinic of Aleppo University Hospital in separated

*Zuhair Al Jaffal, MD; Chief Resident of Department of Ophthalmology at Aleppo University Hospital, Aleppo, Syria. E-mail: Aljaffalzuhair@gmail.com.

*Ammar Kayyali, MD; CIS, Chief of Department of Ophthalmology at Aleppo University Hospital, Aleppo, Syria.

days were included in this study and examined by the same ophthalmologist. A detailed evaluation including ophthalmic and general history, slit lamp biomicroscopy, intraocular pressure measurement, gonioscopy and dilated eye examination were performed. Patients with pseudoexfoliative material on the anterior lens surface and/or the pupillary margin in either or both eyes were labeled as having PXF.

Results: Out of the 500 patients included, eight (1.6%) patients had PXF. Out of 870 eyes included, ten (1.14%) eyes had PXF. The age-adjusted prevalence of PXF in those ≥ 40 years was 0.97% (95% CI: 0.28-1.67) when calculated using the Syrian population as a standard, and 1.34% (95% CI: 0.38-2.30) when calculated using the WHO world population as a standard. Mean age of PXF group was 71.50 years (SD 7.91, range 58-83 years). PXF was bilateral in 25% of cases. It was significantly associated with cataract, glaucoma and hearing loss. Of the PXF patients, 87.5% had cataract, 37.5% had glaucoma and 37.5% had hearing loss.

Conclusions: Pseudoexfoliation appears to be an important disorder in older individuals in Syria because it is associated with increased risk for developing glaucoma, cataract and hearing loss.

INTRODUCTION

Pseudoexfoliation syndrome (PXF) was first reported by Lindberg in 1917 in a Finnish population.¹ It is characterized by the deposition of a distinctive fibrillar material in the anterior segment of the eye,² Figure 1. Pseudoexfoliation syndrome is frequently associated with open angle glaucoma, known as pseudoexfoliation glaucoma, which is the most common identifiable form of secondary open angle glaucoma worldwide.² Pseudoexfoliation is a known risk factor for developing cataracts.³ Complicating factors such as poor mydriasis, zonular weakness, corneal endothelial dysfunction, higher rate of vitreous loss, capsular phimosis, and opacification have all been reported after cataract surgery.^{4,5}

Pseudoexfoliation is considered to be a systemic disorder. Pseudoexfoliative material has been reported in lungs, skin, liver, heart, kidney, gallbladder, blood vessels, extra ocular muscles and meninges.⁶ An

association between PXF and sensorineural deafness has been reported.⁷⁻¹¹

Pseudoexfoliation is rarely seen before the age of 40, and its prevalence increases markedly with age.¹² Although it occurs in virtually every area of the world, a considerable racial variation exists. Epidemiological studies of PXF have been done in some areas in the Middle East, but there is no data available on prevalence of PXF in Syria.

Aleppo University Hospital (AUH) is the most populous governorate medical center of Aleppo. The aim of this hospital-based study is to estimate the prevalence of PXF, provide a descriptive analysis and assess whether PXF is associated with cataract, glaucoma, hearing loss, diabetes mellitus and systemic arterial hypertension.

METHODS

A total of 500 patients aged 40 years or older attending the general ophthalmic clinic of Aleppo University Hospital in the period from September 2014 to June 2015 in separated days were included in this study and examined by the same ophthalmologist. The study protocol was approved by the medical ethics committee of Aleppo University.

Relevant details in medical and ocular history were obtained from each patient including; history of systemic arterial hypertension, diabetes mellitus, hearing loss, intraocular surgery, visual problems, amblyopia and use of corrective glasses and/or contact lenses. All patients underwent complete ocular examination conducted by a senior experienced ophthalmologist included slit lamp biomicroscopy, intraocular pressure measurement, gonioscopy, and dilated fundus examination.

Pseudoexfoliation was diagnosed clinically by the presence of typical pseudoexfoliation material (PXM) at the pupil border on undilated examination, on anterior lens capsule on dilated examination, or on the trabecular meshwork on gonioscopy, with or without Sampaolesi's line and pigment deposition in angle and/or corneal endothelium.²

The diagnosis of cataract was based on clinical biomicroscopy and classified into cortical, nuclear, and posterior subcapsular cataract.¹³

Glaucoma was defined according to the criteria of the International Society of Geographical and Epidemiological Ophthalmology (ISGEO) classification scheme.¹⁴ In that definition, criteria for a category 1 diagnosis (structural and functional evidence) were a vertical cup/disc diameter ratio (VCDR) or an inter-eye asymmetry in the VCDR of ≥ 97.5 th percentile for the normal population, or a neuroretinal rim width reduced to ≤ 0.1 VCDR (between 11 to 1 o'clock or 5 to 7 o'clock), in addition to a definite visual field defect consistent with glaucoma. Criteria for the category 2 diagnosis (advanced structural damage with unproven visual field loss) were a VCDR or a VCDR asymmetry ≥ 99.5 th percentile for the normal population. Criteria for a category 3 diagnosis (for eyes the optic nerve head of which could not be examined or for which a visual field examination was not possible) were a visual acuity $< 3/60$ combined with either an intraocular pressure > 99.5 th percentile, or definite glaucoma medical records such as filtering surgery history.¹⁴

Any eye with previous cataract surgery, history of severe ocular trauma, uveitis, corneal scars, and any other ocular pathology that could have led to inability of examining the anterior capsule was excluded. Any patient whose both eyes met exclusion criteria was excluded from the study.

The statistical analysis was performed using the Statistical Program for the Social Sciences Version 19.0 (SPSS, Inc, Chicago, IL, USA). Means, standard deviations (SDs) and 95% confidence intervals (CIs) were obtained. A p-value of < 0.05 , measured by Pearson's Chi-square test, was considered to indicate statistical significance.

Patients were divided into two groups; PXF and non-PXF. For each group the sex distribution, mean age and standard deviation (SD) were calculated. The total number of eyes studied was 870. The PXF group included 10 eyes and the non-PXF group included 860 eyes. Frequencies of cataract, glaucoma, hearing loss,

diabetes mellitus and systemic arterial hypertension in both groups were estimated.

RESULTS

Out of 500 patients enrolled, 8 were diagnosed with PXF. Thus the prevalence of PXF in those ≥ 40 years was 1.6%. The age-adjusted prevalence of PXF in those ≥ 40 years was 0.97% (95% CI: 0.28-1.67) when calculated using the Syrian population as a standard, and 1.34 (95% CI: 0.38-2.30) when calculated using the WHO world population as a standard Table 1. Out of 870 eyes included, ten (1.14%) eyes had PXF.

			Low CI	High CI
40-44	40 (0)	0.00	0.00	9.22
45-49	46 (0)	0.00	0.00	8.02
50-54	62 (0)	0.00	0.00	5.95
55-59	81 (1)	1.23	0.03	6.88
60-64	96 (0)	0.00	0.00	3.84
65-69	84 (2)	2.38	0.29	8.60
70-74	38 (1)	2.63	0.07	14.66
75-79	21 (3)	14.29	2.95	41.75
80-84	15 (1)	6.67	0.17	37.14
>85	17 (0)	0.00	0.00	21.70
500 (8)				
Crude		1.60	0.69	3.15
Adjusted (Syrian)		0.97	0.28	1.67
Adjusted (WHO World)		1.34	0.38	2.30

Table 1. Age distribution and age adjusted prevalence of PXF in study group.

Of the 8 PXF patient included, 2 (25%) were females and 6 (75%) were males. The association between PXF and gender was not statistically significant ($p=0.288$).

Mean age of PXF group was 71.50 years (SD 7.91, range 58-83 years). Mean age of non-PXF group was 59.76 years (SD 10.97, range 40-94 years). Prevalence of PXF increased with age and was highest among subjects aged > 60 years.

Unilateral PXF was noted in 75% of the PXF group and bilateral PXF was noted in 25%.

Cataract was found in 87.5% of eyes with PXF, but in only 46.5% of non-PXF eyes ($p < 0.029$), indicating a strong association between cataract and PXF, Table 2, Figure 2.

Glaucoma was found in 37.50% of eyes in the PXF group, but in only 2.4% of eyes in the non-PXF group. The association between PXF and glaucoma was statistically significant ($p < 0.001$) Table 2, Figure 2.

Hearing loss was documented in 37.5% of PXF

patients and in only 2.4% of non-PXF. This association between PXF and hearing loss was statistically significant ($p < 0.001$), Table 2, Figure 2. Diabetic was found in 12.50% of patients in the PXF group, and in 16.3% of patients in the non-PXF group. The association between PXF and diabetes mellitus was statistically insignificant ($p < 1.0$). Systemic arterial hypertension was found in 37.5% of PXF group, and in 24.0% non-PXF group. The association between PXF and Arterial hypertension was statistically insignificant ($p < 0.40$), Table 2, Figure 2.

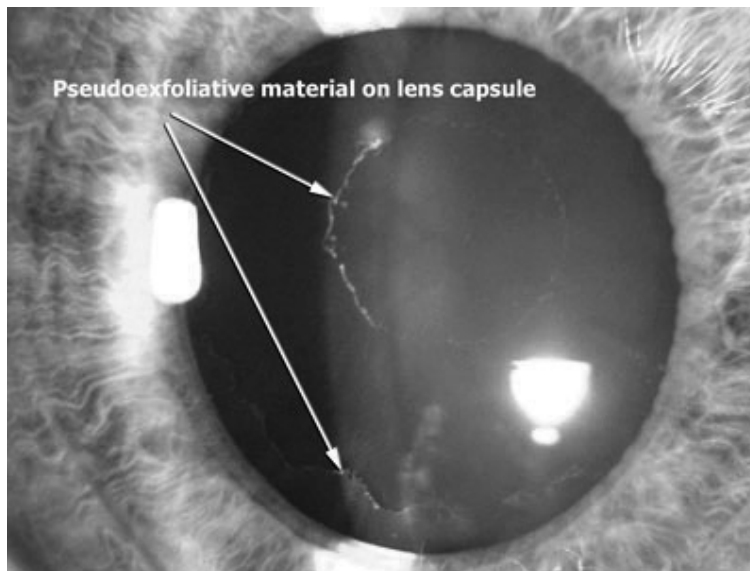
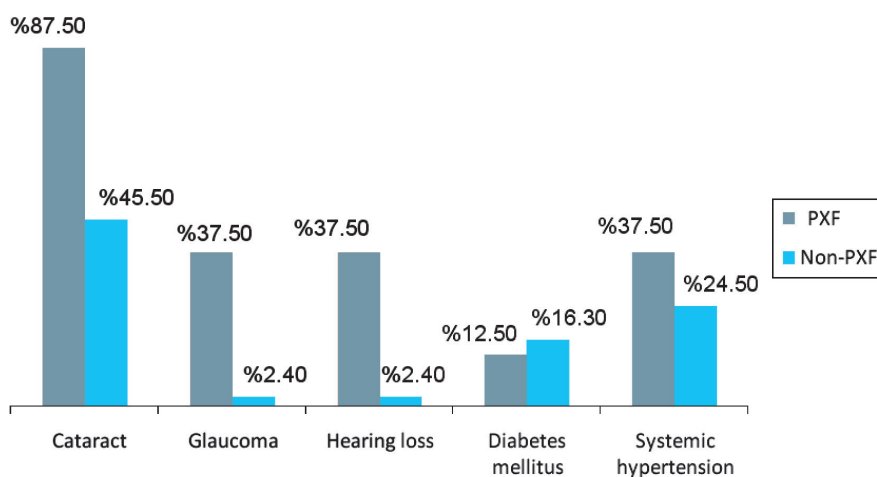


Figure 1. An eye with pseudoexfoliation showing the dandruff like pseudoexfoliation material on the surface of the lens capsule.



PXF=Pseudoexfoliation.

Figure 2. Prevalence of cataract, glaucoma, hearing loss, diabetes mellitus, systemic hypertension among PXF vs non-PXF group.

	PXF, n (%)	Non-PXF, n (%)	p-value
Cataract			
Present	7 (87.5)	229 (46.5)	<0.029
Absent	1 (12.5)	263 (53.5)	
Total	8 (100)	492 (100)	
Glaucoma			
Present	3 (37.5)	12 (2.4)	<0.001
Absent	5 (62.5)	480 (97.6)	
Total	8 (100)	492 (100)	
Hearing loss			
Present	3 (37.5)	12 (2.4)	<0.001
Absent	5 (62.5)	480 (97.6)	
Total	8 (100)	492 (100)	
Diabetic			
Present	1 (12.5)	80 (16.3)	<1.0
Absent	7 (87.5)	412 (83.7)	
Total	8 (100)	492 (100)	
Arterial hypertension			
Present	3 (37.5)	118 (24.0)	<0.40
Absent	5 (62.5)	374 (76.0)	
Total	8 (100)	492 (100)	

PXF=Pseudoexfoliation.

Table 2. Association between PXE and the studied parameters.

DISCUSSION

The reported prevalence rate of PXF syndrome in different populations shows extensive variations. Prevalence rates of as low as 0% in Eskimos,¹⁵ and as high as 38% in Navajo Indians were reported.¹⁶ Framingham study showed that the prevalence of PXF was 1.8%.¹⁷ Prevalence in Icelanders over 60 years were 21%.¹⁵ In northern/western European countries including England, Germany, and Norway prevalence of 4.0%, 4.7%, and 6.3% have been reported respectively.¹⁸

In a hospital based study conducted in Egypt, the prevalence of pseudoexfoliation among patients between 40-90 years was 4.14%.¹⁹ In another hospital based study conducted in Jordan, the prevalence of pseudoexfoliation among patients aged 40-90 years was 9.1%.²⁰ In another study from Yemen the point prevalence of PXF among patients undergoing cataract surgery was 19.53%.²¹

To the best of the authors' knowledge, there are no previous reports on the prevalence or characteristics of PXF in Syria. The prevalence of pseudoexfoliation among individuals aged 40 years or older in this study is 1.6%. The prevalence of pseudoexfoliation among examined eyes of patients aged 40 years or older in this study is 1.14%.

One of the limitations of this study is being a hospital-based rather than a population-based study. Over or under-estimation of the prevalence of PXF and or comorbidities associated with PXF may be attributed to the hospital based nature of the study.

In agreement with findings in other reports, our study showed an increase in the prevalence of PXF with advancing age.²²⁻²⁴

PXF was more common among males (6) than in females (2). A similar finding was reported in the prevalence of PXF among patients Egypt¹⁹ and Yemen;²¹ but the association between PXF and gender was not statistically significant. In a series by Kozart and Yanoff, pseudoexfoliation syndrome was 3 times more common in women than in men.²⁵

We found that PXF was bilateral in (25%) of cases, but in Egypt it was bilateral in the majority of cases (82.2%).¹⁹ Pseudoexfoliation syndrome typically presents unilaterally, why this occurs remains unknown. Pseudoexfoliation material can almost always be demonstrated in fellow eyes on electron microscopy and conjunctival biopsy. In a series by Henry et al, the cumulative probability of a normal fellow eye developing PEX increased over time, with a 6.8% cumulative probability in 5 years and a 16.8% cumulative probability in 10 years.²⁶

A significant association between PXF and cataract was also found in our study and is compatible with findings in other studies.^{23,24}

The age-adjusted PXF rate (direct standardization using the population estimates for the Syria and WHO population as the standard) in our study population for those 40 years of age or older was Approximately similar to the Framingham Eye Study (1.9%)¹⁷ and

Visual Impairment Study (0.98%);²⁷ and lower than the rates the age-standardized rates of PXF reported in south India (3.01%) reported by Thomas et al,²⁸ in the Chennai study (4.9%)²³ and Blue Mountains Eye Study (2.3%).²² However, the age-specific standardized PXF rates in other population-based studies, one from southern India,²⁹ central Iran³⁰ and from Crete (Greece)³¹⁻³² were high (7.6%, 9.4% and 16.1% respectively) in comparison to those in our study.

A strong relationship between glaucoma and PXF is known.²⁶ Subjects with PXF had a two to threefold increased risk for glaucoma according to the Blue Mountains Eye Study.²² Other studies have demonstrated that eyes with PXF had higher mean IOP than eyes without PXF.^{13,27} Moreover, Topouzis F et al. reported increased likelihood of glaucoma at the same IOP in subjects with PXF.³³ Our study is consistent with the above as we found an increased risk for glaucoma in patients with PXF. Our finding that 37.50% of eyes with PXF had glaucoma reflects a comparable proportion to that reported by Al-Bdour et al. in Jordan,²⁰ and Tarek A Shazly et al. in Egypt,¹⁹ yet higher than found by the Blue Mountains Eye Study, which found incidences of 14.2%.²² This finding may reflect an overestimation, which is one of the limitations of hospital-based studies.

One of the limitations of our study is that hearing loss was assessed via detailed history taking. Some of the patients had audiometry documented sensorineural hearing loss, while others didn't undergo audiometric studies. Systemic hypertension was diagnosis with only one record or via detailed medical history and hypertensive retinopathy in funduscopy which aren't enough to make the diagnosis.

In our study hearing loss was found in 37.5% of PXF patients. This association between PXF and hearing loss was statistically significant. Cahill et al. reported that a large proportion of patients with PXF have sensorineural hearing loss in comparison to age-matched controls, regardless of whether or not there is associated glaucoma.⁷ This was confirmed by other studies from different Saudi Arabia, Canada, Turkey and Iran.⁸⁻¹¹ Furthermore, in a recent study Turgut et al. reported high prevalence of asymptomatic vestibular dysfunction among patients with PXF.³⁴

Although the material reported here has many limitations, it adds some new information on the prevalence and characteristics of PXF in a region where data on PXF are scarce.

CONCLUSIONS

In conclusion we found the prevalence of PXF among Syrians individuals attending ophthalmology clinic aged 40 years or older to be 1.6%. This rate is similar to other studies conducted in Visual Impairment Study (0.98%), but lower than other studies conducted in other Middle Eastern countries in Egypt (4.14%) and Jordan (9.1%). Population-based study should be performed to plan and tackle its complications, namely, cataract and glaucoma. Ophthalmologists in Syria should focus on the detection of PXF, especially considering the risks for operative complications related to PXF and the higher prevalence of glaucoma among PXF patients.

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