Prevalence of Pseudoexfoliation syndrome and its association with specific ocular diseases in sample of Iraqi patients Attending Ibn Al-Haithem Teaching Hospital for eye diseases

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ABSTRACT

INTRODUCTION: Pseudo exfoliation syndrome (PXF) is an age related disease characterized by deposition of abnormal materials of extracellular fibrils in many ocular organs. It is autosomal dominant inheritance with incomplete penetrance and variable expressivity. It is the most common identifiable cause of secondary open angle glaucoma

OBJECTIVE: To estimate the prevalence of pseudoexfoliation syndrome in visitors, patient and healthy, attending Ibn Al-Haithem Teaching Hospital for Eye Diseases. And evaluate its association with glaucoma specific ocular diseases.

METHODS: A Cross-sectional study carried out on (1150) participants aged from 40 to 90 years who attended the out-patient department at Ibn Al-Haithem Teaching Hospital for eye diseases from May 2013 to April 2014. Pseudo- exfoliation syndrome was diagnosed by the presence of a typical pseudoexfoliative material on anterior lens surface and /or pupillary margin in either or both eyes on a slit-lamp examination. Glaucoma was searched for in all participants to define association with the PXF.

RESULTS: Out of the 1150 patients included, 119 (10.34 %) patients had PXF. The mean age of PXF group was 71.6±9.8 years with a range of 42 – 86 years. The prevalence of PXF was found to be increased with advancing age (P= 0.0001) but had no gender predilection (P=0.08). PXF was bilateral in 6.26 % of cases and unilateral in 4.08% but this was statistically insignificant (P>0.05). Cataract was found in 83 patients (69.7 %) of PXF group while glaucoma was found in 40 patients (33.6 %) of PXF group. .

CONCLUSION: PXF is an age dependent disorder with no appreciable gender predilection. The overall prevalence was 10.34% in this study. PXF has a significant association with cataract and secondary glaucoma..

Key words: pseudoexfoliation syndrome, cataract, glaucoma.

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INTRODUCTION

Pseudoexfoliation syndrome (PXF) is an age-related disease characterized by widespread deposition of abnormal extracellular fibrillar material on many ocular and extra-ocular tissues. The reported prevalence of PXF varies extensively from 0% to more than 40%,[1-3] PXF was first described by a Finnish ophthalmologist named John Lindberg in 1917 in his doctoral thesis.[4] Dvorak-Theobald felt that this disorder is not a true exfoliation of the lens capsule, but rather represents precipitates of an unknown substance that are deposited on the anterior lens capsule and other structures in the anterior ocular segment. She recommended the term "pseudo-exfoliation of the lens capsule," to distinguish the condition from capsular delamination or "true" exfoliation, and the term pseudo-exfoliation syndrome is commonly used in modern literature.[5]

The composition and origin of the deposited material is not entirely clear and it is most prominent on the anterior lens capsule and at the pupillary margin.[6] Similar material has also been detected in skin and connective tissue portions of various visceral organs.[7,8] It is thought to be

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an ocular manifestation of a systemic disorder in which an extracellular fibrillar material accumulates in many ocular and systemic tissues.[7-12]

A hereditary transmission of this disorder is not yet clarified. However, it was suggested that it is transmitted by an autosomal dominant gene with incomplete penetrance and variable expressivity.[13] There are two major theories on the pathogenesis of PXF syndrome. The first links the exfoliation fibres to the elastic microfibrils of the elastic system,[14, 15] the second theory considers PXF to be a generalized disorder of the basement membranes.[8,16-21]

PXF has been associated with cataract progression, increased intraocular pressure and intraoperative complications like zonular or posterior capsular rupture, vitreous loss and luxation of intraocular lens implants. It is the most common identifiable cause of secondary open-angle glaucoma which characterized by worse prognosis than primary open angle glaucoma; rapid progression and higher resistance to medical therapy.[22]

There is a high prevalence of PXF in Arabic populations. In Saudi Arabia, Summanen and Tonjum has reported that the prevalence of pseudoexfoliation syndrome is 13%[23]. In Oman, PXF was the cause of half of the cases of glaucoma.[24] Many epidemiological studies in the middle east have measured the prevalence of PXF;[25,26] however, data from Iraq is scarce, triggering us to do this study. The aim of this study was to measure the prevalence of pseudoexfoliation syndrome (PXF) among Iraqi people with or without eye disease who attended Ibn Al-Haithem Teaching Hospital for eye diseases in Baghdad and to find its associated with cataract and glaucoma.

METHODS

Settings and study design: A total of (1150) patients aged from 40 – 90 years who attended the out-patient department at Ibn Al-Haitham Teaching Hospital for eye diseases from May 2013 to April 2014 were included in the study.

Ethical issues: The study was conducted according to the ethical approval obtained from the hospital. All participants in this study have been asked to provide their agreement and written consents were obtained after explaining the aims and the nature of the study.

Definition of the cases and Inclusion and exclusion criteria: All visitors, patients with eye diseases and their companions, who attended the outpatient clinic at Ibn Al-Haitham Teaching Hospital for Eye Diseases during the studied period were included in this study. Patients with aphakia or pseudophakia were excluded from this study due to difficulty in making the diagnosis. Similarly, patients with only eye or those having one phthisical eye as a result of previous trauma were excluded to avoid calculation errors.

Sampling: We chose only those who fulfilling the inclusion criteria and visiting the outpatient clinic on Mondays of each week during the studied year.

Outcomes: Patient with typical pseudoexfoliative material on the anterior lens surface and / or dandruff at pupillary margin in either or both eyes on slit lamp examination were labelled as having PXF for sake of this study. (**See figure 1**) For those whom their initial slit-lamp examination was negative, a repeated examination was done after using medical pupillary dilation with Tropicamide eye drop 1% instilled to both eyes. The examination was done by one consultant ophthalmologist during the whole period of the study.

Procedure: A detailed ophthalmic history was taken from all participant in addition to a com-

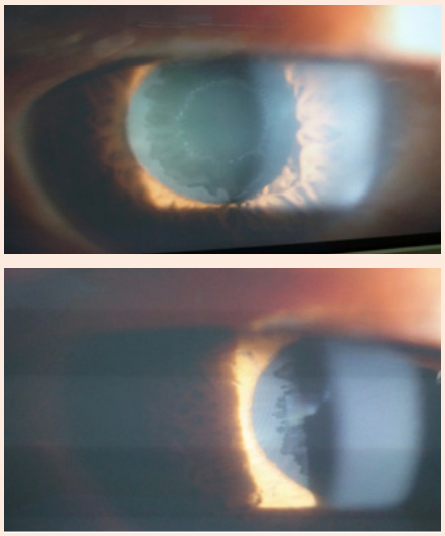

Figure 1: *Upper image* **Showing the three ring zones of PXF.** *Lower image*: **Showing pseudoexfoliative material on anterior lens capsule**

prehensive ophthalmic examination which included visual acuity by Snellen chart, intraocular pressure (IOP) examination by Goldman applanation Tonometer, examination of the anterior segment by slit lamp before and after dilatation, and disc examination with a condensing lens (+90 D) indirect slit lamp biomicroscope.

Those who were labelled as PXF positive participants were examined for the presence of glaucoma which is defined as IOP> 21 mmHg and / or optic disc changes suspected for glaucomatous damage, or eyes with filtration surgery, or use of antiglaucoma medications. If glaucoma was diagnosed then gonioscopic examination using Goldmann's three-mirror system to exclude angle closure glaucoma and other subtypes of open angle glaucoma; pigmentary, uveitic, and neovascular.

Statistics: Patients were divided into two groups: PXF and non-PXF. For each group the age and gender distribution, mean age, standard deviation, range were calculated. Analysis of data was carried out using the available statistical package of SPSS-22 (Statistical Packages for Social Sciences- version 22). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). Statistical significance was considered whenever the P value for the test of significance was equal or less than 0.05.

RESULTS

Out of the 1150 patients included in the study, 119 were diagnosed as having PXF, thus the prevalence of PXF in the whole study group was 10.34%, the sample of data is distributed according to age groups and gender (Table 1). Unilateral PXF was noted in 47 patients (4.08%) of total number of study group and it represents 39.5% of patients in PXF group, while bilateral PXF was noted in 72 patients which represents (6.26%) of the total study group and (60.5%) of PXF group, but it was statistically insignificant (P>0.05). See table 1

The mean age of male patients in the sample studied was 66±9.7 years, range 42 – 86 years) and of female patients was 64.6±11.1 years, range 40 – 87 years) as shown in table 2.

Mean age in the PXF group was 71.6±9.8 years, range 42 - 86 years) as shown in table 3. The prevalence increases with advancing age and this is statistically significant (P=0.0001) as shown in table 3. Of patients with PXF, 75 (63%) were female and 44 (37%) were male. The association between PXF and gender was statistically insignificant (P = 0.080) indicating that there was no gender predilection in this syndrome. (See table 2)

Table 1: Criteria of the patient included in this study.

		No.	%
Age (years)	40---49	97	8.5
	50---59	252	21.9
	60---69	311	27.0
	70---79	404	35.1
	≥ 80	86	7.5
	Mean±SD(Range)	65.2±10.5 (40-87)	
Gender	Male	512	44.5
	Female	638	55.5
PXF	Bilateral	72	6.26
	Unilateral	47	4.08
	No	1031	89.66
Cataract	Yes	677	58.9
	No	473	41.1
Glaucoma	Yes	113	9.8
	No	1037	90.2

Cataract was found in 83 patients (69.7 %) of PXF group but in 594 patients (57.6%) of non – PXF group (P = 0.011), indicating a strong association between cataract and PXF. Glaucoma was found in 40 patients (33.6 %) of PXF group while in 73 patients (7.1 %) of non-PXF group. The association between secondary glaucoma and PXF syndrome was statistically highly significant (P = 0.0001) indicating that PXF had been a risk factor for secondary glaucoma (Table 4).

DISCUSSION

Although pseudoexfoliation occurs in every race, its prevalence varies considerably between countries and even between regions or ethnic groups within same country.[27]

This variation is apparently due to:

1. Differences within the populations that have been studied. Geographic and ethnic differences appear to be important factors, with high prevalence in Scandinavian countries and among people of Mediterranean origin.

Table 2: Distribution of sample studied according to Gender.

		Male		Female		P value
		No.	%	No.	%	
Age (years)	40---49	34	3.0	63	5.5	0.017*
	50---59	117	10.2	135	11.7	
	60---69	158	13.7	153	13.3	
	70---79	172	15.0	232	20.1	
	≥80	31	2.7	55	4.8	
	Mean±SD(Range)	66.0±9.7 (42-86)		64.6±11.1 (40-87)		
PXF		44	37	75	63	0.214

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

Table 3: Distribution of sample studied in relation to PXF.

		PXF		Non PXF		Total (%)	P value
		No.	%	No.	%		
Age (Years)	40---49	3	3.1	94	96.9	97 (100)	0.0001*
	50---59	10	4.0	242	96.0	252 (100)	
	60---69	28	9.0	283	91.0	311 (100)	
	70---79	43	10.65	361	89.35	404 (100)	
	≥80	35	40.7	51	59.3	86 (100)	
Mean±SD (Range)		71.6±9.8 (42-86)		64.5±10.4 (40-87)			
Gender		Male	44	37	468		45.4
	0.080	Female	75	63	563		54.6

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

Table 4: Association of PXF with cataract and glaucoma.

	PXF		None PXF		P value
	No.	%	No.	%	
Present	83	69.7	594	57.6	0.011*
Absent	36	30.3	437	42.4	
Present	40	33.6	73	7.1	0.0001*
Absent	79	66.4	958	92.9	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

2. Depending on the diagnostic criteria used by the authors.
3. Whether or not the examination is carried out under mydriasis.

Prevalence rates of as low as 0% in Eskimos,[2] and as high as 38% in Navajo Indians[28] were reported. In our study we found a prevalence of 10.34 %, this may reflect an overestimation of the true prevalence because this was a hospital–based rather than a population–based study and it is nearly similar to the prevalence data reported from neighbouring countries which may reflects racial or geographical factors.

In a hospital based study conducted in Jordan, the prevalence of pseudoexfoliation among patients aged 40-90 years was 9.1%.[26] A study that was conducted at the Gaziosmanpasa University Hospital in Turkey between December 2007 and December 2008 revealed a prevalence rate of 12.2%.[29] A population-based survey among Saudis comprising 376 persons aged 40 years or more showed an overall pseudoexfoliation prevalence of 9.3%.[23] In a new study from Central Iran, 13.1% pseudoexfoliation syndrome was observed in people aged 50 years or more.[30]

In the United States, pseudoexfoliation syndrome is less common, with one study revealing a prevalence of 1.6% for a population over 30 years, and 3.2% for those over 60 years,[31] and other studies were showing prevalence rates of 0.67% for ages 52-64 years, 2.6% for 65-74 years, and 5.0% for 75 - 85 years respectively.[13] In consistence with all previous report, [32– 36] we observed that prevalence of PXF increases with advancing age. Although the reasons behind this are unknown, some speculate that the changes in gene expression which occurs with advancing age may be a cause.[37]

Conflicting reports exist regarding the association between gender and prevalence of pseudoexfoliation. In our study, there was no gender predilection, a similar findings was reported in a study conducted in Jordan[26] and other countries,[33,34] in contrast, studies conducted in Egypt and Yemen have found that the prevalence of PXF is more common in male,[38,39] while the Blue Mountains Eye study has shown an increased prevalence of pseudoexfoliation in female.[32]

Regarding laterality in our study, PXF was bilateral in 72 patients (6.26%) of total number of study group; the finding which is similar to that of other studies,[34] although again this result was statistically insignificant.

A significant association between pseudoexfoliation and cataract is apparent in our study, emphasizing the reports of other stud-

ies.[33,34,40,41] The association of PXF to secondary glaucoma is well established[30] and a strong relationship between glaucoma and PXF is known.[42] Subject with PXF had a two to three folds increased risk for secondary glaucoma according to the Blue Mountains Eye Study.[32] Other studies have demonstrated that eyes with PXF had higher mean IOP than eyes without PXF.[13,32] Our study has shown that 33.6 % of those with PXF have secondary glaucoma; a similar finding has been found in a study from Jordan.[26]

Due to some logistic limitations regarding time, human and financial resources, we include only those person, diseased or not, who visited our hospital. A community based study is required to draw a better conclusion about the prevalence of PXF in our community and figure out its real effect on development of some eye diseases especially cataract and glaucoma.

CONCLUSION

PXF is an age dependent disorder with no appreciable gender predilection. The overall prevalence of PXF syndrome was 10.34%. and a significant association was found with cataract and secondary glaucoma.

REFERENCES

1. Ringvold A. Epidemiology of the pseudo-exfoliation syndrome. *Acta Ophthalmol Scand* 1999; 77: 371 – 375 .
2. Forsius H. Prevalence of pseudoexfoliation of the lens in Finns, Lapps, Icelanders, Eskimos and Russians. *Trans Ophthalmol Soc UK* 1979; 99: 296 – 298.
3. Forsius H. Exfoliation syndrome in various ethnic populations. *Acta Ophthalmol Suppl* 1988; 184: 71–85.
4. Lindberg JG: Kliniska undersokningar over depigmenteringen av pupillarranden och genomlysbarheten av iris vid fall av aldersstarr samt i normala ogon hos gamla personer. [Clinical studies of depigmentation of the pupillary margin and transillumination of the iris in cases of senile cataract and also in normal eyes in the aged] [Thesis] Helsinki, Finland:Helsinki University; 1917
5. Dvorak-Theobald G. Pseudo-exfoliation of the lens capsule. Relation to "true" exfoliation of the lens capsule as reported in the literature and role in the production of glaucoma capsulocuticulare. *Am J Ophthalmol* 1954; 37(1): 1-2.
6. Prince AM, Ritch R. Clinical signs of the pseudoexfoliation syndrome. *J Ophthalmology* 1986; 93: 803-7.
7. Schlötzer-Schrehardt UM, Koca MR, Naumann GO, et al. Pseudoexfoliation syndrome. Ocular manifestations of a systemic disorder. *Arch Ophthalmol* 1992; 110: 1752-1756.
8. Streeten BW, Li ZY, Wallace RN. Pseudoexfoliative fibrillopathy in visceral organs of a patient with pseudoexfoliation syndrome. *Arch Ophthalmol*. 1992; 110: 1757-1762.
9. Streeten BW , Dark AJ, Wallace RN, Li ZY and Hoepner JA: Pseudoexfoliative fibrillopathy in the skin of patients with ocular pseudoexfoliation. *AM J Ophthalmol* 1990; 110: 490 – 499.
10. Schlötzer-Schrehardt UM, Von der Mark K, Sakai LY & Naumann GO : Increased extracellular deposition of fibrillin – containing fibrils in pseudoexfoliation syndrome. *Invest Ophthalmol Vis Sei* 1997;38: 970 – 984.
11. Naumann GO, Schlötzer-Schrehardt U & Kuchle M: Pseudoexfoliation syndrome for the comprehensive ophthalmologist. Intraocular and systemic manifestation. *Ophthalmology* 1998;105:951 – 968.
12. Netland PA, Ye H, Streeten BW & Hernandez MR: Elastosis of the lamina cribrosa in pseudoexfoliation syndrome with glaucoma. *Ophthalmology* 1995; 102: 878 – 886
13. Hiller.R, Sperduto. RD, Krueger. DE. Pseudoexfoliation, intraocular pressure, and senile lens changes in a population-based survey. *Arch Ophthalmol J*. 1982; 100(7): 1080-2 .
14. Garner, A., & Alexander, R.A. Pseudoexfoliative disease: histochemical evidence of an affinity with zonular fibres. *British Journal of Ophthalmology* 1984; 68(8): 574-580.
15. Streeten BW, Gibson SA, and Dark AJ. Pseudoexfoliative material contains an elastic microfibrillar-associated glycoprotein. *Transactions of the American Ophthalmological Society* 1986;84: 304-317.
16. Dickson DH, and Ramsay MS. Fibrillopathia epitheliocapsularis (pseudoexfoliation): a clinical and electron microscope study. C*anadian Journal of Ophthalmology* 1975;10(2): 148-161.
17. Eagle Jr RC, FontRL, and Fine BS. The basement membrane exfoliation syndrome. *Archives of Ophthalmology* 1979; 97(3): 510-515.
18. Harnisch JP, Barrach HJ, Hassell JR, and Sinha PK. Identification of a basement membrane proteoglycan in exfoliation material. *Graefe's Archives for Clinical and Experimental Ophthalmology* 1981;215(4): 273-278.
19. Konstas, A.G., Marshall, G.E., & Lee, W.R. Immunogold localisation of laminin in normal and exfoliative iris. *British Journal of Ophthalmology* 1990; 74(8): 450-457.
20. Kubota, T., Khalil, A., Tawara, A., Zhang, X., & Inomata, H. Double staining of proteoglycans and the HNK-1 carbohydrate epitope in pseudoexfoliation material. *Current Eye Research* 1998;17(1):60-64.
21. Tawara, A., Fujisawa, K., Kiyosawa, R., & Inomata, H. Distribution and characterization of proteoglycans associated with exfoliation material. *Current Eye Research* 1996;15(11): 1101-1111.
22. Ritch R, Schlötzer-Schrehardt U. Exfoliation syndrome. *Survey of Ophthalmology* 2001; 45 (4): 265-315.
23. Summanen P, Tönjum AM. Exfoliation syndrome among Saudis. *Acta Ophthalmol Suppl* 1988; 184: 107 – 111.
24. Bialasiewicz AA, Wali U, Shenoy R, Al-Saeidi R. Patients with secondary open-angle glaucoma in Pseudoexfoliation (PEX) syndrome among a population with high prevalence of PEX. Clinical findings and morphological and surgical characteristics. *J Ophthalmology*. Nov 2005;102(11):1064-8.
25. Al-Shaer M, Bamashmus M, Al-Barrag A. Point prevalence of pseudoexfoliation syndrome in patients scheduled for cataract surgery in eye camps in Yemen. *Middle East Afr J Ophthalmol* 2010; 17(1):74-7.
26. Al-Bdour MD, Al-Till MI, Idrees GM, Abu Samra KM: Pseudoexfoliation syndrome at Jordan University Hospital. *Acta Ophthalmol* 2008; 86(7): 755-757.
27. Vesti E, Kivelä T. Exfoliation syndrome and exfoliation glaucoma. *Progress in Retinal and Eye Research* 2000; 19(3): 345-368.
28. Faulkener HW: Pseudoexfoliation of the lens among Navajo Indians. *Am J Ophthalmol* 1971; 72: 206-7.
29. Cumurcu T , Kilic R, Yologlu S. The frequency of pseudoexfoliation

syndrome in the middle Black Sea region of Turkey. ***Eur J Ophthalmol***. 2010; 20(6): 1007-11.

30. Nouri-Mahdavi K, Nosrat N, Sahebghalam R, Jahanmard M. Pseudoexfoliation syndrome in central Iran: a population-based survey. ***Acta Ophthalmol Scand***. 1999 Oct; 77(5): 581-4.
31. Cashwell, LF, Shields, MB: Exfoliation syndrone. Prevalence in a southeastern United States population. ***Arch Ophthalmol J***. 1988; 106: 335.
32. Mitchell P, Wang JJ, Hourihan F: The relationship between glaucoma and pseudoexfoliation: The Blue Mountains Eye Study. ***Arch Ophthalmol*** 1999; 117: 1319-1324.
33. Arvind H, Raju P, Paul PG, Baskaran M, Ramesh SV, George RJ, McCarty C, Vijaya L. Pseudoexfoliation in South India. ***Br J Ophthalmol*** 2003; 87:1321-1323.
34. Tiliksew T, Kefyalew R: Prevalence of pseudoexfoliation in Ethiopian patients scheduled for cataract surgery. ***Acta Ophthalmol Scand*** 2004; 82: 254-258.
35. American Academy of Ophthalmology; Basic and clinical science course. 2011 – 2012; 10: 103 – 104.
36. Aasved H. Mass screening for fibrillopathia epitheliocapsularis, so – called senile exfoliation or pseudoexfoliation of the anterior lens capsule. ***Acta Ophthalmol (Copenh)*** 1971; 49(2): 334 – 343.
37. Karger RA, Jeng SM, Johnson DH, Hodge DO & Good MS: Estimated incidence of pseudoexfoliation syndrome and pseudoexfoliation glaucoma in Olmsted Country, Minnesota. ***J Glaucoma*** 2003; 12: 193 – 197.
38. Shazly TA, Farrag AN, Kamel A, Al-Hussaini AK. Prevalence of pseudoexfoliation syndrome and pseudoexfoliation glaucoma in Upper Egypt. ***BMC ophthalmology***. 2011 Dec;11(1):18.
39. Al-Shaer M, Bamashmus M, Al-Barrag A: Point prevalence of pseudoexfoliation syndrome in patients scheduled for cataract surgery in eye camps in Yemen. ***Middle East Afr J Ophthalmol*** 2010; 17(1): 74-7.
40. Thomas R, Nirmalan PK, Krishnaiah S: Pseudoexfoliation in southern India:the Andhra Pradesh Eye Disease Study. ***Invest Ophthalmol Vis Sci*** 2005; 46(4): 1170-6.
41. Kuchle M, Ambery A, Martus P, Nguyen NX & Naumann GO. pseudoexfoliation syndrome and secondary cataract. ***Br J Ophthalmol*** 1997; 81: 862 – 866.
42. Henry JC, Krupin T, Schmitt M, Lauffer J, Miller E, Ewing MQ, Scheie HG. Longterm follow-up of pseudoexfoliation and the development of elevated intraocular pressure. ***Ophthalmology*** 1987; 94: 545-552.

Abbreviation list: Intraocular pressure (**IOP**), Millimetre of Mercury (**mmHg**), Pseudoexfoliation syndrome (**PXF**), Statistical Packages for Social Sciences (**SPSS**)

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