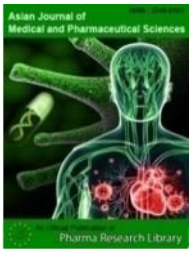
Asian Journal of Medical and Pharmaceutical Sciences
ISSN: 2348-0165
Journal Home Page: www.pharmaresearchlibrary.com/ajmps



Research Article

Clinical correlation between Pattern of pseudoexfolative Deposits and its Severity of Glaucoma in Iraq

Ali Naji Alsharifi[1*], Yaser A.R. Naseer Alkhafaji[2], Noor Raad Kareem[3]

[1]*CAB Ophthalmologist, Glaucoma consultant, Ibn al-Hatim teaching Hospital, Baghdad, Iraq*
[*2]*M.B.Ch.B., CABOph (Arab board), FICO, MRCSEd (Ophthalmology), College of Medicine, Mustansiriyah University, Baghdad, Iraq*
[3]*M.B.Ch,B.,CABM Ophthalmology, Kerbala University College of Medicine, Karbala, Iraq*

Abstract

Background: Pseudoexfoliation syndrome (PEX) is characterized by the accumulation of pseudoexfoliative material (PXF) in ocular tissues. Early diagnosis and timely management of PEX are crucial since it is the leading cause of secondary glaucoma in Iraq. **Aim:** To review current perspectives on the pattern of PXF deposits and evaluate their possible clinical correlation with the severity of glaucoma in the Iraqi population. **Methods:** Demography and medical history of participants were noted in a case report form. Subjects underwent visual acuity measurement, subjective refraction, and central corneal thickness (CCT) measurement by optical method. Intraocular pressure (IOP) was measured by Goldman applanation tonometry. A slit-lamp examination of each eye was conducted before and after the instillation of mydriatic eye drops. Patients were evaluated by a glaucoma specialist to confirm pseudoexfoliation glaucoma (PEG). Further, clinical correlation was done between the pattern of PXF deposits (whether capsular–dominated or pupillary-dominated) with the severity of glaucoma. Statistical data were entered in Microsoft Excel 2016. . Statistical analysis was done using SPSS V24 software where the chi-square test. P value <0.05 was considered as statistically significant. **Results:** A total of 79 patients' 113 eyes with PEX were examined for the presence of PEG. The mean age was 65.66 ± 6.003 years (50-83years). PEX was more common in females [n=61(53.98%)] than in males [n=52(46.02%)]. The correlation between the pattern of PXF deposit on anterior segment structure and PEG was not statistically significant (P=0.205). Severe glaucoma was significantly associated with capsular-dominated PXF deposits compared to pupillary-dominated PXF deposits (40.7% vs 15.6%) with P=0.014. Capsular-dominated PXF deposits were significantly associated with good pupillary dilatation (45.7% vs 18.8%) as compared to pupillary-dominated PXF deposits with a P=0.01. **Conclusion:** The findings demonstrate that PEX with capsular-dominated PXF shows an increased risk of severe glaucoma over the pupillary-dominated deposits. Also, good pupillary dilatation is significantly associated with a capsular pattern of PXF deposits. Larger multicentre studies are needed to confirm these findings and apply the results towards better eye health outcomes.

Keywords: Pseudoexfoliation syndrome (PEX), pseudoexfoliative glaucoma (PEG), pseudoexfoliative material (PXF), intraocular pressure, open-angle glaucoma.

Article Info

Corresponding Author
Ali Naji Alsharifi
CAB Ophthalmologist,
Glaucoma consultant,
Ibn al-Hatim teaching Hospital, Baghdad, Iraq

Article History: Received 11 April 2023, **Accepted** 18 May 2023, **Published online** 16 July 2023

Citation: Ali Naji Alsharifi*, et al. Clinical correlation between Pattern of pseudoexfolative Deposits and its Severity of Glaucoma in Iraq*. *A. J. Med. Pharm, Sci.*, 2023, 11(1): 07-12.

C o n t e n t s

1. Introduction

Pseudoexfoliation syndrome (PEX) is a common extracellular matrix condition caused by ageing andis usually linked to serious chronic secondary open-angle glaucoma. Lindberg, a Finnish ophthalmologist, was the first to describe PEX in 1917. The term "pseudoexfoliation syndrome" was given by Dvorak-Theobald, later in 1954.The build-up of fluffy, white, amyloidal, proteinaceous material in the eye serves as a tell-tale sign of PEX. Deposition of the pseudoexfoliative or flaky fibrillar material (PXF) commonly occurs on sites such as anterior surface of the iris, trabecular meshwork, anterior capsule of the lens and sometimes the cornea and anterior chamber and its angle. PEX is a common reason for chronic open-angle glaucoma, also known as pseudoexfoliation glaucoma (PEG), which is relatively difficult to treat.[1–4]

The epidemiology of PEX varies based on sex, age, and ethnic origin. The incidence of PEX is greater in women and increases with age. The prevalence progressively increases among different categories as follows: individuals over 50yrs of age; glaucoma patients; ocular hypertensives; glaucoma patients admitted to the hospital; glaucoma patients undergoing surgery; and patients with absolute glaucoma or who are blind from glaucoma. While PEX is more common in females, males are at greater risk of PEG if they have PEX.[3,5]

Globally, the prevalence of PEX for individuals over the age of 60 is roughly 10-20%, and it increases to about 40% for individuals over the age of 80.[6]Al-Saffar and Ahmed, conducted a cross-sectional study in 2019 in the Kurdistan region of Iraq and Kirkuk city –of Iraq. This study included 378 patients (756 eyes) aged 50 years or older detected with PEX. A detailed evaluation showedthat 58 (15.3%) had PEG.[7]

PEX can be diagnosed clinically using a slit lamp examination by visualizing the deposit of white, dandruff-like PXF on the iris and the anterior lens capsule pupillary margin.[2]Changes in the iris are also a well-recognized early clinical feature of PEX. However, the most noticeable appearance of PXF is at the pupillary border adjacent to the lens. PXF deposition on the iris sphincter and at the pupillary margin, along with loss of pigment in the pupillaryruff, is another common key feature of PEX diagnosis. Pigment accumulation on the cornea may cause diffuse and specific pigmentation on the central endothelium, rarely having the pattern of a Krukenbergspindle.[1]

PEX maybe unilateral or bilateral. It is strongly correlated with elevatedintraocular pressure (IOP) found in 44% patients and may lead to PEG or open-angle glaucoma. Thus, it can be the most popular identifiable trigger of secondary open-angle glaucoma. PEX can also cause complications in cataract surgery as it may lead to poor dilation of eyes and lens zonules becoming unstable. This may also increase the risk of complications such as zonular dialysis, capsular bag rupture, and loss of vitreous.[2]

The conversion of PEX to PEG occurs at the rate of 5% in patients having PEX for 5 years, 15% at 10 years and 60% for patients having PEX since 15 or more years. PEG is more severe than primary open angle glaucoma (POAG). It is also linked with an elevated risk of higher IOP, higher IOP fluctuations, increased glaucoma medication resistance, and blindness.[6]

The PXF tend to block the spaces within the trabecular meshwork, which might promote the deposition of cellular debris and pigment. This can result in blocking the outflow of aqueous humour into Schlemm's canal. This might be the reason for elevation of IOP to chronic levels leading to PEG. In unilateral PEX, the exfoliative eye has an IOP of roughly 2 mm Hg higher in comparison to the non-PEX eye.[3]

PEX has recently been also identified to trigger chronic open-angle glaucoma and angle-closure glaucoma, blood-aqueous barrier impairment, lens subluxation and vision-threatening conditions at the time of cataract extraction, like zonular dialysis, capsular rupture and vitreous loss. PEX might also be a risk factor in cataract surgery as it increases the weakness of the zonular apparatus and reduces pupillary dilatation.[3,8]

The pattern of PXF deposits and their clinical correlation with the severity of glaucoma has not been extensively evaluated earlier. This study implies the possibility to provide evidence for the same. Thus, the study is a timely

intervention and aims to review current perspectives on the pattern of PXF deposits and their clinical correlation with the severity of glaucoma in patients with PEX. It aims to address the management of ocular and systemic associations of this clinically important and biologically fascinating disease.

2. Methodology

Study Design: An observational cross-sectional study was conducted at a tertiary hospital called the Ibn Haitham Hospital outpatient consultation clinic in Iraq, from April 2020 to January 2021. 113 eyes of total 79 patients with PEX were examined for the presence of PEG. Details like the pattern of deposits on the anterior lens capsule, the presence of pupillary abnormalities and their correlation with the severity (indices) of glaucoma were analysed. The study adhered to the tenets of Declaration of Helsinki. The Ministry of Health, Supervising Committee of the Arab Board of Medical Specializations in the Republic of Iraq has approved the study.

Patients meeting the following inclusion criteria, attending the outpatient clinic in Ibn Haitham Hospital were included:

1. Age >45 years old.
2. Male and female patients.
3. Slit lamp examination of anterior segment that revealed PXF materials deposited either on the lens capsule or pupillary border.

Exclusion criteria were as follows:

1. Aphakia or pseudophakia.
2. Media opacity, e.g., mature cataract, corneal scar, vitreous opacity
3. Any optic neuropathy other than glaucomatous optic neuropathy.
4. Pathologic myopia.
5. Patients with a history of ocular trauma

Sample size

113 eyes of 79 patients with PEX were included in the study. In this study, interviewer-administered questions covered demography, medical history including diabetes, hypertension, or other medical diseases; medication use like systemic beta-blocker; and ocular history. Subjects underwent visual acuity measurement, subjective refraction,, slit-lamp examination of the anterior segment of the eye, followed by dilated fundus examination. The laterality of the disease was recorded as right, left, or bilateral.IOP was measured by Goldman applanation tonometry and central corneal thickness (CCT) was measured by an optical method.

A slit-lamp examination of each eye was performed before and after the instillation of mydriatic agents (one drop of tropicamide 1% augmented by one drop of phenylephrine 10% instilled after 5 minutes). The anterior segment of each eye was scanned, looking for signs of PXS, including the presence of exfoliative material on the anterior lens surface or pupillary margin.Pupil size was measured after instillation of mydriatic agent and was classified as either well- (>4mm), or poorly- (< or equal 4mm) dilated pupil,using the numerical scale on the slit lamp.

PEX was diagnosed by the presence of typical white PXF deposits on the pupillary border or the anterior lens surface, often in different zones. The pattern of these deposits is classified basis the predominant site of deposits being either capsular-dominated (CD-PXF) or pupillary-dominated (PD-PXF).

Lens capsule depositswere classified as follows: peripheral capsular deposits, central and peripheral capsular deposits (target sign or double ring sign),and heavy central or peripheral capsular deposits with elevated edges of the flakes from the lens capsule surface.Pupillary border observations were classified as follows: deposits scatteredaround the pupillary border, deposits incompletely surrounding the pupillary border,and deposits completely surroundingthe pupillary border.

All patients were referred to a glaucoma clinic in Ibn Al Haitham Eye Teaching Hospital, where PEG was either confirmed or excluded by a glaucoma specialist depending on the criteria of glaucoma that included measurement of IOPand CCT, gonioscopicand optic disc examination, optical coherence tomography of optic nerve head and visual field examination.

A clinical correlation between the pattern of PXF deposits with the severity of glaucoma was done. Statistical analysis methods were introduced into Microsoft Excel 2016.Post purification and revision, data were analysed using SPSS V24.Descriptive statistics were presented as tables and graphs, while inferential statistics were analysed using the chi-square test to find the significance of the association between categorical variables. P value <0.05 was considered as statistically significant.

3. Results and Discussion

A total of 79 patients provided 113 eyes.The minimum age was 50 years, and maximum was 83 years. The patients had a mean age of 65±6.003 year as seen in Table 1. PEX was more common in females 61 (53.98%) than males52 (46.02%). Bilateral involvement was seen in 34 (30.1%) patients, right eye unilaterality was seen in 23 (20.4%) patients and left eye unilaterality in 22 (19.5%) patients.

Discussion

The primary objective of this studywas to evaluate the correlation between the pattern of PXF deposits and severity ofPEG. It also aimed to evaluate any association between pupillary dilatation and the pattern of PXF deposits. This is becausecurrently there is no way to identify which cases ofPEXare at risk of developing severe glaucoma or PEG. Although there is a non-significant

association between the prevalence of glaucoma in general,withthe predominant pattern of PXF deposits, our study showeda statisticallysignificant association between the prevalence of severe PEG and capsular-dominated pattern of PXF deposits.

The underlying mechanism of glaucomatous optic neuropathy is mainly elevated IOP, which is mediated by the accumulation of PXF deposits in the extracellular matrix of the trabecular meshwork. This accumulation causes structural and functional disturbances in the trabecular meshwork, leading to its clogging and reducing the outflow of aqueous humour. Ultimately, this results in increased IOP and can lead to the development of glaucoma.

The possible explanation for our results is that in cases of CD-PXF deposits,the surface of the lens is rough.With good pupillary dilatation and normal movement of the pupil, there is frequent shedding of PXF material.Iris pigment epithelial cells are also shed from the movement of the iris on the lens, clogging the trabecular meshwork with subsequent elevation of IOP and eventually, glaucomatous optic neuropathy.In cases of PD-PXF, there is poor pupillary dilatation,leading to little or no movement of the iris, and therefore, only mildor no glaucoma.

Tojo and colleagues found that PEG patients were more likely to have peak IOP during the daytime whereaspatients without PEGexperienced peak IOP at night.This correlated with our study findings that patients who had CD-PXF deposits with good pupillary dilatation and movement, may show high IOP with fluctuation and severe glaucoma, due to high movement of the pupil mostly occurring during the daytime. This will not happen in the PD-PXF deposits due to poor dilatation, lesser lens movement and subsequently, none or mild glaucoma.[9]

Our explanation for poor pupillary dilatation is the iris vasculopathy and this, by itself due to ischemia, could lead to decreased movement of the iris. Study findings are consistent with previous research results. Shuba *et al*. found that there was a statistically non-significant correlation between all markers of glaucoma and the anterior lens capsule PXF material. Still, that study did not take into consideration the severity of glaucoma.[10] Another study by Lee *et al*concluded that as the accumulatedPXF material builds up in the angle and clogs the trabecular meshwork, the IOP rises and induces glaucomatous optic neuropathy.[11] Another explanation for our finding is that there may be another factorcontributing to elevated IOP and secondary glaucoma (other than the amount of PXF materials),represented by exaggerated pigmentdeposition seen in eyes with PEX, either due to a defect in the iris or liberated from the iris because of rubbing of iris pigment epithelium against the rough anterior lens capsule.However, our study does not estimate the amount of the pigment deposited on different anterior segment structures, including trabecular meshwork,to correlate it with the presence of glaucoma.

Shuba *et al*., also found a significant correlation between iridocorneal angle pigmentation and IOP elevation in PEX.[10]Similarly, Puska*et al*.concludedthat the degree of pigmentation,is a more important risk factor for elevated IOP and glaucoma, than the amount of exfoliation,.This too correlates with our results that the patient with PD-PXF deposits and poor pupillary dilatation is shedding lesser iris pigment due to lesserlens movement and iris atrophy.[12]

In another study, Moreno-Montanes *et al* found a significant correlation between the increment of IOP and the degree of diffuse pigmentation in the trabecular meshwork and the presence of the Sampaolesi line.[13]

In addition to the mechanisms mentioned above, an important question that comes to mind when one tries to explain the PEG is whether the glaucomatous damage was only IOP-mediated through PXF material and/or pigment deposition in the trabecular meshwork and Schlemm canal, orareother non-IOP-mediated mechanisms related to PEX and can be regarded as independent risk factors for glaucoma.[13]In a study, Conway *et al*.reported that even though it is most widely held that obstruction to trabecular outflow is the major mechanism of PXF open-angle glaucoma,the effectof juxtacanalicular endothelial cell dysfunction,increased aqueous protein level and abnormalities ofthe elastic tissue of lamina cribrosa, are also possible contributors and reflect our incomplete understanding of the condition.[14]

Elastosis affecting the lamina cribrosa might be a pathogenetic factor, as Netland*et al*. concluded that the elastosis observed in eyes with PEX was more severe than in eyes with POAG; glaucomatous optic nerve damage is more likely to develop in patients with ocular hypertension (OHT) and PEX than in those with OHT without PEX.[15] Al-Saffar and Ahmed conducted anothercross-sectional study in Iraq. They concluded that PEX was related to significant glaucoma risk in Iraq, at 15.3% prevalence. Further,OHT was prevalent at 9%. They recommended that the focus of ophthalmologists in Iraq should be more on the detection of PEX and to evaluate IOP in PEX patients, keeping in mind the possible risks for operative complications in PEX and the high prevalence of PEG. [7] Similarly, based on our findings and limitations of being a single-centre study, we recommend more localised studies focusing on the prevalence of PEX in Iraq to help understand the epidemiology of PEX. Since PEX is a risk factor for glaucoma, patients with PEX must be regularly examined to provide an early diagnosis of PEG and timely interventions.

Table 1: Demographic characteristics for patients with pseudoexfoliation syndrome

Variable	Mean±SD
Age	65±6.003
M:F	52:61
R:L	23:22

Table 2 below shows that PXF deposits were capsular-dominated compared to pupillary-dominated [n=22 (33.33%) vs n=44 (66.67%)] in PEX patients without PEG. Similarly, the PXF deposition was more capsular-dominated than pupillary-dominated [n=37 (78.72%) vs n=10 (21.27%) even in in PEX patients with PEG. Thus, there is no statistically significant association between the pattern of PXF deposits and the presence of PEG(p= 0.205).

Table 2: Analysis of presence of PEG in correlation with capsular- or pupillary-dominated PXF deposits

Pattern of PXF deposits			Final diagnosis		
			Normal (no glaucoma)	PEG	Total
Domination	capsular	Count	44	37	81
		% within domination	54.3%	45.7%	100.0%
	pupillary	Count	22	10	32
		% within domination	68.8%	31.3%	100.0%
Total		Count	66	47	113
		% within domination	58.4%	41.6%	100.0%

PEG; pseudoexfoliation glaucoma, PXF; pseudoexfoliation flaky fibrillar material

Table 3: Correlation between pattern of PXF deposits and glaucoma severity

Pattern of PXF deposits			Glaucoma severity		
			No/mild/moderate glaucoma	Severe glaucoma	Total
Domination	capsular	Count	48	33	81
		% within domination	59.3%	40.7%	100.0%
	pupillary	Count	27	5	32
		% within domination	84.4%	15.6%	100.0%
Total		Count	75	38	113
		% within domination	66.4%	33.6%	100.0%

PXF; pseudoexfoliation flaky fibrillar material

Severe glaucoma was significantly associated (p = 0.014) with capsular-dominated PXF deposits compared to pupillary-dominated PXF deposits (40.7% vs 15.6%) as seen in Table 3 above.

Table 4: Analysis of PXF deposit pattern and pupillary dilatation

Pattern of PXF deposits			Pupil dilatation		
			Well	Poor	Total
Domination	capsular	Count	37	44	81
		% within domination	45.7%	54.3%	100.0%
	pupillary	Count	6	26	32
		% within domination	18.8%	81.3%	100.0%
Total		Count	43	70	113
		% within domination	38.1%	61.9%	100.0%

PXF; pseudoexfoliation flaky fibrillar material

Capsular-dominated PXF deposits were significantly associated (p=0.01) with good pupillary dilatation (45.7% vs18.8%)as compared to PD-PXF deposits.

4. Conclusion

PEX with capsular-dominated PXF shows an increased risk of developing severe glaucoma as compared to the pupillary pattern of PXF deposits. Further, good pupillary dilatation is significantly associated with a capsular pattern of PXF material deposits. In conclusion, a thorough and regular ocular and systemic examination is a must for PEX

patients for timely PEG determination and management in Iraqi population.

5. Acknowledgement

We would like to thank Mumbai-based Spellbound Inc. for the timely publication support tothe authors. The publication assistance for drafting the manuscript was paid for.

Funding

No funding was received during the conduct of this study

Declaration of interest

The author reports no conflict of interest with respect to research or publication of this manuscript.

6. References

[1] Tekin K, Inanc M and Elgin U (2019) Monitoring and management of the patient with pseudoexfoliation syndrome: Current perspectives. Clinical Ophthalmology Volume 13: 453–464.

[2] Tuteja S and Chawla H (2023) *Pseudoexfoliation Syndrome and Glaucoma*. StatPearls [Internet]. Bookshelf ID: NBK574522 PMID: 34662036

[3] Ariga M, Nivean M and Utkarsha P (2013) Pseudoexfoliation syndrome. *Journal of Current Glaucoma Practice* 7(3): 118–120.

[4] Nobl M and Mackert M (2019) Pseudoexfoliation Syndrome and Glaucoma. *KlinischeMonatsblätter für Augenheilkunde* 236(09): 1139–1155.

[5] Plateroti P, Plateroti AM, Abdolrahimzadeh S, et al. (2015) Pseudoexfoliation syndrome and pseudoexfoliation glaucoma: A review of the literature with updates on surgical management. *Journal of Ophthalmology* 2015: 1–9.

[6] Palko JR, Qi O and Sheybani A (2017) Corneal alterations associated with pseudoexfoliation syndrome and glaucoma: A literature review. *Journal of Ophthalmic and Vision Research* 12(3): 312.

[7] Al-Saffar AA and Ahmed DM (2019) The prevalence of glaucoma among pseudoexfoliation syndrome patients. *Saudi Journal of Medical and Pharmaceutical Sciences* 05(10): 856–864.

[8] Drolsum L, Ringvold A and Nicolaissen B (2007) Cataract and glaucoma surgery in pseudoexfoliation syndrome: A Review. *Acta Ophthalmologica Scandinavica* 85(8): 810–821.

[9] Tojo N, Hayashi A, Otsuka M, et al. (2016) Fluctuations of the intraocular pressure in pseudoexfoliation syndrome and normal eyes measured by a contact lens sensor. *Journal of Glaucoma* 25(5).

[10] Shuba LM, Doan AP, Maley MK, et al. (2007) Diurnal fluctuation and concordance of intraocular pressure in glaucoma suspects and normal tension glaucoma patients. *Journal of Glaucoma* 16(3): 307–312.

[11] Lee RK (2008) The molecular pathophysiology of pseudoexfoliation glaucoma. *Current Opinion in Ophthalmology* 19(2): 95–101.

[12] Puska P (2009) The amount of lens exfoliation and chamber-angle pigmentation in exfoliation syndrome with or without glaucoma. *Acta Ophthalmologica Scandinavica* 73(3): 226–232.

[13] Montañés JM, Alonso AQ, Serna AA, et al. (n.d.) Exfoliation syndrome: clinical study of the irido-corneal angle. *Journal FrancaisD'ophtalmologie* 13(4): 183–188.

[14] Conway RM, Schlotzer-Schrehardt U, Kuchle M, et al. (2004) Pseudoexfoliation syndrome: Pathological manifestations of relevance to intraocular surgery. *Clinical and Experimental Ophthalmology* 32(2): 199–210.

[15] Netland PA, Ye H, Streeten BW, et al. (1995) Elastosis of the lamina cribrosa in pseudoexfoliation syndrome with glaucoma. *Ophthalmology* 102(6): 878–886.