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Analytical Study Of Pseudoexfoliation Syndrome, Its Association With Glaucoma, And Its Surgical Complications.

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ABSTRACT

Pseudoexfoliation (PXF) is an age-related disorder characterized by the accumulation of fibrillar extracellular material in ocular tissues and is often associated with glaucoma. To clinically analyze cases of pseudoexfoliation syndrome, its association with glaucoma, and its surgical complications. 100 patients with pseudoexfoliation syndrome who attended the Government Tirunelveli Medical College Hospital between November 2021 and September 2022 were included in the study. Patients with the presence of exfoliation material on the pupillary margin and/ or lens capsule were included in the study. Patients with a previous history of trauma and anterior uveitis were excluded. Also, patients with POAG and primary angle closure glaucoma, other secondary glaucomas, uncontrolled diabetes, and IHD were excluded. All were subjected to detailed anterior segment examination, fundus examination, and glaucoma workup. Surgical complications were analyzed in patients undergoing cataracts and combined surgery and followed up periodically. The most common age group was 61-70 years. 66% were males and 34% were females. 74% of patients had bilateral pseudoexfoliation and 24% had unilateral pseudoexfoliation. 48 (48%) patients with pseudoexfoliation had glaucoma most common being open angle glaucoma (32 cases). Poor pupillary dilatation was noted in 58% of patients. 45.97% of eyes with pseudoexfoliation had nuclear cataracts and 38.50% had cortical cataracts. In 50 eyes that were operated for cataracts, 30 (60%) eyes had poor pupillary dilatation. 8 (16%) eyes had corneal endothelial touch, and 8 (16%) eyes had posterior capsular rent and vitreous loss out of which 7 eyes had poor dilatation. 7 (14%) eyes had zonular dehiscence. PCIOL was placed in 43 (86%) eyes after sufficient surgical modifications. 58% had visual acuity in the range between 6/60-6/18. In 18 eyes that underwent combined surgery, 10 (55.55%) eyes had advanced glaucoma. 6 eyes had the corneal endothelial touch, 2 (11.11%) eyes had posterior capsular rent, and 3 (16.6%) eyes had zonular dialysis. All these eyes with complications had poor dilatation. PCIOL was implanted in 16 eyes. Post op vision was < 6/60 in 38.8% eyes. 72.22% of eyes had IOP < 20mmHg after surgery. Bilateral pseudoexfoliation was more common with a male preponderance. The presence of pseudoexfoliation is associated more with open-angle glaucoma. Surgical complications like corneal endothelial touch, posterior capsular rent, and zonular dialysis were noted more in cases with poor dilatation. Adequate surgical modifications will give a good visual outcome. Combined surgery is a good option in pseudoexfoliation eyes with glaucoma.

Keywords: Phacoemulsification, cataract, complications; plasmapheresis, pseudoexfoliation glaucoma, pseudoexfoliation syndrome, secondary glaucoma.

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INTRODUCTION

Pseudoexfoliation syndrome is an age-related disease in which abnormal fibrillar extracellular material of uncertain origin accumulates in many ocular tissues [1]. Polymorphism of exon1 of the LOXL1 gene has been found in patients with pseudoexfoliation syndrome. It is recognized as a common cause of secondary open-angle glaucoma [2]. Deposition of amorphous grey dandruff-like material on the anterior lens surface is the most consistent and important diagnostic feature of pseudoexfoliation syndrome. Exfoliative material is also deposited on the corneal endothelium, trabecular meshwork, iris, pupillary margins, zonules, ciliary processes, and anterior hyaloid phases [3]. The presence of pseudoexfoliation is associated with increased risks of intraocular surgery, most commonly zonular dehiscence, capsular rupture, and vitreous loss during cataract extraction [4]. Pseudoexfoliation syndrome is associated with secondary open-angle glaucoma in 50% of cases. The exact mechanism of the rise of IOP is not clear but is proposed due to the clogging of trabecular meshwork with exfoliation material and pigments [5]. Glaucoma in pseudoexfoliation syndrome has a worse prognosis due to poor response to medications and complications involved in surgical management [6,7].

MATERIALS AND METHODS

100 patients with pseudoexfoliation syndrome who attended the Government Tirunelveli Medical College Hospital between November 2021 and September 2022 were included in the study. Presence of exfoliation material on the pupillary margin and/or lens. All the patients were subjected to a detailed slit lamp examination and the following signs were looked for Conjunctiva-congestion, Cornea-edema, pigmentation, exfoliation material, Anterior chamber depth-flare, cells, depth exfoliation material, pigment dispersion. Iris-pattern, transillumination defects, iridodonesis. Pupil size, reaction to light, exfoliation material, dilatation with mydriatics. Lens-exfoliation material, cataractous or not, phacodonesis, subluxation, or dislocation of the lens. The pupil was dilated as a routine in most of the cases to note the three zones of exfoliation material on the lens capsule. Fundus was examined with direct ophthalmoscopy and slit lamp biomicroscope to look for glaucomatous changes in the disc. Glaucoma workup was done for all patients, which included Gonioscopy with Goldmann single mirror lens, Tonometry using Goldmann applanation tonometer, and automated perimetry with octopus 301 in selected cases. During gonioscopy, the presence of exfoliation material and increased trabecular pigmentation were also noted. In patients undergoing cataract or combined surgery, A-scan, and K reading were noted and IOL power was calculated by the SRK 2 formula. Routine investigations like blood sugar, urine albumin sugar, and blood pressure measurements were done.

Exclusion Criteria: Previous history of trauma, Anterior uveitis, Secondary cataract, primary open and closed angle glaucoma, Other secondary glaucoma, uncontrolled hypertension, and ischemic heart disease.

RESULTS

Table 1: Age Distribution

Age (years)	No. of cases
41-50	6
51-60	34
61-70	43
71-80	17

In our study, out of 100 cases, 6 cases presented between 41-50 years, 34 cases between 51-60 years, 43 cases presented between 61-70 years, and 17 cases between 71-80 years. Thus the most common age group was between 61-70 years followed by 51-60 years. The mean age of the patients was 63.71 years. Out of the 100 cases with pseudoexfoliation, 66 (66%) were males and 34(34%) were females.

Table 2: Laterality

	No. of cases	%	No. of eyes
UL	26	26	26
BL	74	74	148
Total	100	100	174

74(74%) cases had bilateral pseudoexfoliation and 26(26%) had unilateral pseudoexfoliation. Thus, a total of 174 eyes out of 100 patients had pseudoexfoliation

Table 3: Glaucoma Association

Pseudoexfoliation syndrome	No. of cases	%
With glaucoma	48	48%
Without glaucoma	52	52%

Out of the total 100 patients with pseudoexfoliation, 48(48%) patients had glaucoma while 52(52%) had no glaucoma. The incidence of glaucoma in pseudoexfoliation varies from 20-85% in the literature.

Table 4: Sex incidence-glaucoma

	pseudoexfoliation with glaucoma		pseudoexfoliation without glaucoma		Total	
	No	%	No	%	No	%
Males	40	60.60	26	39.39	66	100
Females	8	23.52	28	76.42	34	100

Males showed a higher predominance in pseudoexfoliation glaucoma than females.

Table 5: Type of glaucoma

Type of glaucoma	No. of patients	%
Open Angle Glaucoma	32	66.66
Angle Closure Glaucoma	16	33.33
Total	48	100

Among the 48 patients with glaucoma, 32(66.66%) had open-angle glaucoma and 16(33.33%) had angle closure glaucoma. Thus open angle glaucoma is more common in pseudoexfoliation syndrome.

Open-angle glaucoma**Table 6A: Open-angle glaucoma Laterality**

Open-angle glaucoma	No. of cases	%
Unilateral	12	37.50
Bilateral	20	62.5
Total	32	100

Table 6B: Unilateral open-angle glaucoma

Unilateral open-angle glaucoma	No. of cases
With bilateral pseudoexfoliation	4
With unilateral pseudoexfoliation	8
Total	12

Out of the 32 cases of open-angle glaucoma, 20(62.50%) cases had bilateral open-angle glaucoma

and 12 cases (37.50%) had unilateral open-angle glaucoma. Out of the 12 cases with unilateral open-angle glaucoma, 4 had pseudoexfoliation in both eyes, but glaucoma only in one eye. These patients are at high risk of developing glaucoma in the fellow eye and hence require regular follow-up.

Table 7: laterality of angle closure glaucoma

	No. of cases	%
Unilateral	7	43.75
Bilateral	9	56.25
Total	16	100

Out of the 16 cases with angle closure glaucoma, 9 had bilateral angle closure glaucoma and 7 had unilateral angle closure glaucoma. Among the 7 unilateral cases, 2 cases had secondary angle closure due to subluxated lens. There was no history of trauma in any case of subluxation. Thus, the subluxation evidenced by phacodonesis and iridodonesis is due to exfoliation material causing zonular weakness and hence pseudoexfoliation is attributed as the cause of angle closure glaucoma. In the remaining 5 cases of unilateral exfoliation and 9 cases of bilateral exfoliation, there was no secondary factor other than pseudoexfoliation. The fellow eyes also had shallow anterior chambers in unilateral cases. These patients are likely to have primary angle closure glaucoma with co-existing pseudoexfoliation. Pseudoexfoliation may be the cause of aggravating angle closure glaucoma.

Table 8: Optic nerve damage in glaucoma

Optic nerve head	No damage (no. of eyes)	Early glaucomatous damage (no. of eyes)	Advanced glaucomatous damage (no. of eyes)	Total (no. of eyes)
Open-angle glaucoma	9	24	22	52
Angle-closure glaucoma	11	7	7	25

Out of the 52 eyes with open-angle glaucoma, no optic nerve damage was seen in 9(17.30%) eyes, early glaucomatous damage was seen in 24(46.15%) eyes, and advanced glaucomatous damage in 22(42.30%) eyes. Out of the 27 eyes with angle closure glaucoma 11(40.74%) showed no damage, 7(25.92%) eyes showed early damage and 7(25.92%) eyes showed advanced glaucomatous damage. Thus advanced glaucomatous optic nerve damage is noted more in open-angle glaucoma.

Table 9: Clinical features

	Features	No of patients
Conjunctiva	pterygium	5
Cornea	Pigmentation	6
	Spheroidal degeneration	3
Anterior Chamber	Exfoliation material	2
Iris	Pupillary ruff defects	52
	Iridodonesis	10
Pupil	Poor dilatation	58
	Exfoliation material	99

5 patients had Pterygium and 3 patients had spheroidal degeneration. The associated occurrence of these features suggests a common etiology of ultraviolet light. 58 patients had poor pupillary dilatation. This is a recognized entity in pseudoexfoliation syndrome due to intrinsic degenerative changes occurring in the sphincter papillae.

Table 10: Lens status

Type	No. of eyes
Clear lens	2
Nuclear cataract	80
Cortical cataract	
Immature cataract	57
Mature cataract	7
Hypermature cataract	3
Subluxated cataract	13
Pseudophakia	10
Aphakia	1
Decentered IOL	1
Total	174

80(45.97%) eyes had nuclear cataracts, while cortical cataract was seen in 67(38.70%) eyes. 13 eyes had subluxated lenses as characterized by phacodonesis and iridodonesis. Majority of patients had visual acuity <6/60 due to the presence of associated cataracts and glaucoma. Almost all cases had increased trabecular hyperpigmentation. It was also seen in the fellow eye of unilateral cases and pigmentation was more on the eye with raised tension in bilateral cases. The trabecular hyperpigmentation of the fellow eye in unilateral cases could be a preclinical sign of exfoliation syndrome. In the majority of cases, fields were not possible due to poor vision. Automated perimetry was done in selected cases. All patients were advised periodic reviews.⁴ Patients had diabetes mellitus, and 8 patients had systemic hypertension which was under control with medications.

Table 11: Pupillary diameter

	<6mm	>6mm	Total
Cataract	30	20	50
Combined surgery	10	8	18

They advocated that small pupils could be enlarged by prosthetic and non - prosthetic methods. Non - prosthetic techniques include visco-mydriasis, manual iris stretching, and iris microspherotomies. Prosthetic techniques include iris hooks and the use of pupil expansion devices.

Table 12: IOL implantation

IOL	No. of eyes	%
PCIOL	43	86
SFIOL	1	2
Aphakia	6	12

43(86.00%) eyes were implanted with PCIOL after employing various surgical modifications like sphincterotomy (7 eyes) and iris hook (1eye) to mechanically dilate the pupil, and manual anterior vitrectomy in cases of PCR. One (2%) eye was implanted with SFIOL following zonular dehiscence and 6(12%) eyes were left aphakic due to the above-mentioned complications.

Table 13: Association of complications in cataract surgery with pupillary diameter

Complication	No. of eyes	Pupillary dilatation			
		<6mm		>6mm	
		No	%	No	%
Corneal endothelial touch	9	6	66.66	3	33.33
Zonular dehiscence	7	7	100	0	0
Posterior capsular rent	8	7	87.50	1	12.5

Out of the 6 eyes with corneal endothelial touch, 4(66.66%) had poor pupillary dilatation (< 6mm) and 2(33.33%) had good pupillary dilatation (> 6mm). Out of 3 eyes with zonular dehiscence and 2 eyes with posterior capsular rent, all (100%) had poor pupillary dilatation.

Table 14: Post-op visual acuity

Post op visual acuity	1 st post-op week		Follow up after one month	
	No of eyes	%	No of eyes	%
6/18-6/6	11	22	18	36
6/60-6/18	31	64	29	58
PL-6/60	8	16	3	6

In the first post-op week, post-op visual acuity of 6/18-6/6 was noted in 11(22%) eyes, 6/60-6/18 in 31(64%) eyes, and perception of light to 6/60 in 8(16%) eyes. After one month, post op visual acuity of 6/18-6/6 was noted in 18(36%) eyes, 6/60-6/18 in 29(58.0%) eyes and perception of light to 6/60 in 3(6.0%) eyes. Visual acuity improved in patients with corneal endothelial touch at subsequent follow-up.

Table 15: Indication for combined surgery

	Open-angle glaucoma		Angle-closure glaucoma		Total
	Early glaucoma	Advanced Glaucoma	Early glaucoma	Advanced Glaucoma	
No	5	8	3	2	18
%	27.77	44.44	16.66	11.11	100

Out of the 18 eyes, 13(72.88%) eyes had open-angle glaucoma and 5(27.77%) had angle closure glaucoma. Totally 10(55.55%) had advanced glaucomatous damage of the optic nerve.

Table 16: IOL implantation

IOL	No. of eyes	%
PCIOL	16	88.88
Aphakia	2	11.11

16(88.88%) eyes were implanted with PCIOL and 2(22.22%) eyes were left aphakic due to the above-mentioned complications.

Table 17: Association of complications in combined surgery with pupillary diameter

Complication	No. of eyes	Pupillary dilatation			
		<6mm		>6mm	
		No	%	No	%
Corneal endothelial touch	6	4	66.66	2	33.33
Zonular dehiscence	3	3	100	0	0
Posterior capsular rent	2	2	100	0	0

Out of the 6 eyes with corneal endothelial touch, 4(66.66%) had poor pupillary dilatation (< 6mm) and 2(33.33%) had good pupillary dilatation (> 6mm). Out of 3 eyes with zonular dehiscence and 2 eyes with posterior capsular rent, all (100%) had poor pupillary dilatation. Out of 3 eyes with one or either or all complications, all (100%) had poor pupillary dilatation.

Table 18: Post-op visual acuity

Post-op visual acuity	1 st post-op week		Follow up after one month	
	No. of eyes	%	No. of eyes	%
6/18-6/6	2	11.11	4	22.22
6/60-6/18	7	38.88	7	38.88
PL-6/60	9	50.00	7	38.88

In the first post-op week, post-visual acuity of 6/18-6/6 was noted in 2(11.11%) eyes, 6/60-6/18 in 7(38.88%) eyes, and perception of light to 6/60 in 9(50.00%) eyes. At subsequent follow-up after one month, visual acuity showed improvement in 4 patients who had corneal endothelial touch as the complication. After one month, post op visual acuity of 6/18-6/6 was noted in 4(22.22%) eyes, 6/60-6/18 in 7(38.88%) eyes and perception of light to 6/60 in 7(38.88%) eyes. Poor visual acuity is mainly due to advanced glaucomatous damage to the optic nerve.

Table 19: Post-op IOP

Post op IOP (mmHg)	1 st post-op week		Follow up after one month	
	No. of eyes	%	No. of eyes	%
<20	12	66.66	17	94.44
20-30	5	27.77	1	5.55
>30	1	5.55	0	0

Post-op IOP during the first post-op week was less than 20mmHg in 12(66.66%) eyes, between 20-30mmHg in 5 eyes (27.77%), and more than 30mmHg in one (5.55%) eye. At subsequent follow-up, 17(94.44%) eyes had IOP less than 20mm Hg of which 4 eyes were on adjuvant topical antiglaucoma medication while 13 were under surgical control without any medication. One (5.55%) case had IOP between 20-30mmHg with antiglaucoma medication. Thus in 13(72.22%) eyes, IOP was less than 20mmHg without any antiglaucoma medication indicating successful IOP control after surgery.

DISCUSSION

100 cases of pseudoexfoliation syndrome reported to our hospital were taken for the study to analyze features of pseudoexfoliation syndrome, its association with glaucoma, and its surgical complications [8]. In this study, the most common age group overall was 61-70 years. In bilateral pseudoexfoliation, the most common age group was 61-70 years, in unilateral pseudoexfoliation the most common age group was 51-60 years. The mean age was 63.71 years and only 6% of the patients were less than 50 years. Hence, exfoliation syndrome is a disease of the elderly. 66% of pseudoexfoliation patients were males and 34% were females [9]. As ultraviolet light is a possible factor related to exfoliation syndrome, the definite male preponderance could be explained partly by the fact that males are more likely to be involved with outdoor activities than females. 74 % of patients had bilateral pseudoexfoliation and 26% had unilateral exfoliation. Thus, bilateral exfoliation being more common could be due to the possibility that the unilateral cases invariably become bilateral at a later date. 48% of exfoliation patients had glaucoma while 52% had no evidence of glaucoma. Thus, there is a definite association between glaucoma in pseudoexfoliation syndrome [10]. The higher incidence of glaucoma, when compared to that in Western studies could be attributed to racial predisposition (Western/ Asian). Of the 48 patients with glaucoma, 32 had open-angle glaucoma and 16 had angle closure glaucoma. Thus open-angle glaucoma is more commonly associated with pseudoexfoliation syndrome [11]. Of 32 patients with open angle glaucoma 12 had glaucoma only in one eye and 20 had glaucoma in both eyes. Out of the 12 patients with unilateral open angle glaucoma 4 had exfoliation in both eyes with glaucoma in one eye. These patients have a higher risk of developing glaucoma in the other eye also and hence were advised periodic review. Out of 20 pseudoexfoliation patients with bilateral open-angle glaucoma all had pseudoexfoliation in both eyes. Of 48 patients with glaucoma 16 had angle closure glaucoma. Of the 16, 2 had secondary angle closure glaucoma (due to subluxated lens). The 2 patients with subluxated lenses had no history of trauma and the subluxation was spontaneous, most probably due to the weakening of zonules due to exfoliation material deposition [12]. Of the remaining 14 patients there was no other secondary cause involved except for the pseudoexfoliation syndrome. These patients are more likely to have Primary angle Closure Glaucoma with pseudoexfoliation syndrome. Pseudoexfoliation syndrome may be the cause or

aggravating factor for angle closure glaucoma, by mechanism of pupillary block which can be caused by anterior shift of the iris-lens diaphragm due to weakened zonules, posterior synechiae, and rigid nondilating pupil [13]. In 58 patient's pupil poor pupillary dilatation following administration of mydriatic agents was noted probably due to intrinsic degenerative changes occurring in sphincter papillae in pseudoexfoliation syndrome. 45.97% of the pseudoexfoliation eyes had nuclear cataracts, while 38.50% had cortical cataracts [14]. In 50 eyes with pseudoexfoliation which were operated on for cataracts, 30 had poor pupillary dilatation following the administration of mydriatic agents [15]. Out of the 50, 8 (16.0 %) eyes had posterior capsular rent. Out of the 8 eyes, 7 (87.50%) of them had poor pupillary dilatation while 1 (12.5 %) of them had good pupillary dilatation. Out of the 8 (16.0 %) eyes with Vitreous loss, 7(87.5%) of them had poor pupillary dilatation while 1 (12.5 %) of them had good pupillary dilatation. All 7 (100 %) eyes with zonular dehiscence had poor pupillary dilatation. In our study, best-corrected post-operative visual acuity of 6/18- 6/6 was seen in 18(36.0%) cases, visual acuity of 6/60 – 6/18 was seen in 29(58%) cases, and visual acuity of perception of light to 6/60 was seen in 3(6.0%) cases.[16] In 18 eyes with pseudoexfoliation which underwent combined surgery, 10 had poor pupillary dilatation following administration of mydriatic agents. 13(72.22%) eyes had open angle glaucoma and 5(27.77%) eyes had angle closure glaucoma. 10(55.55%) eyes had advanced glaucomatous damage of the optic nerve [17]. Out of the 18, 2 (11.11 %) eyes had posterior capsular rent with vitreous loss, and 3(16.6%) eyes had zonular dehiscence. Both eyes with posterior capsular rent and 3 eyes with zonular dehiscence had poor pupillary dilatation. 2 eyes were left aphakic due to the above complications. In our study, postoperative visual acuity of 6/18-6/6 was seen in 22.22% of cases, visual acuity of 6/60 – 6/18 was seen in 38.88% of cases, and visual acuity of perception of light to 6/60 was seen in 38.88% cases [18]. Visual acuity less than 6/60 was mainly due to advanced glaucomatous damage. 17(94.44%) eyes had IOP less than 20mm Hg of which 4 eyes were on adjuvant topical antiglaucoma medication. Thus, in 13(72.22%) eyes, IOP was less than 20mmHg without any antiglaucoma medication indicating successful IOP control after surgery [19,20].

CONCLUSION

PEX syndrome and glaucoma are relatively common diseases that can complicate the lives of patients and eye surgeons. The incidence of PEX syndrome in our cataract patients was 6 %. Proper diagnosis of this disease is important not only for the possible occurrence of numerous complications during and after cataract surgery but also for the possible presence of secondary glaucoma. It also serves to detect possible involvement of the contralateral eye. In addition, due to the involvement of practically all tissues in the body, the patient is endangered by numerous, especially vascular comorbidities. For these reasons, we find it appropriate that these patients are observed by other healthcare specialists. In our experience, early indication of cataract surgery is important to achieve a lower degree of zonular fragility and a softer lens core. In addition, lower levels of proinflammatory pseudo-exfoliation material occur in the anterior segment of the eye in the early stages, which may have a beneficial effect on postoperative healing.

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