Ocular Clinical Spectrum of Pseudoexfoliation in Cataract Patients at a Tertiary Eye Care Centre in Rural Maharashtra – A Cross Sectional Study

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ABSTRACT

BACKGROUND
Pseudoexfoliation (PEX) is a systemic microfibrillopathy characterised by accumulation of gray-white fibrogranular extracellular material over the lens, pupil or cornea. Different clinical variants of PEX in cataract patients are known to occur. We wanted to study the different clinical variants of PEX in cataract patients, the intraoperative and postoperative complications and the visual prognosis of cataract surgery.

METHODS
A total of 100 patients with PEX in cataract were subjected to detailed examination and necessary investigations. Cataract surgery was performed in all patients using the manual small incision cataract surgery (SICS). Vision before and after surgery was recorded. Refraction was done and documented. Best corrected visual acuity was noted and was followed-up postoperatively for 2 – 4 weeks.

RESULTS
Maximum prevalence of PEX (57 %) was seen in 51 - 60 years of age and 64 % were males and 36 % were females. The involvement was bilateral in 53 % and unilateral in 47 % cases. The range of intraocular pressure (IOP) was 12.4 mm Hg to 23.1 mm Hg. 67 % patients had insufficient mydriasis and 81 % cases were found to have PEX material deposited on the peripheral zone and 19 % cases on both peripheral zone and central zone. A total of 27 % cases had mature cataract and 7 % had hypermature cataract.

CONCLUSIONS
PEX requires a thorough preoperative planning along with a proper intraoperative care to ensure an uneventful surgery and a successful postoperative result.

KEYWORDS
Pseudoexfoliation, Mydriasis, Cataract

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BACKGROUND

Pseudoexfoliation (PXF) is a senile systemic microfibrillopathy characterised by collection of gray-white fibrogranular extracellular material produced by abnormal basement membranes of aging epithelial cells.[1] The most distinguishing ocular feature which confirms the diagnosis is the presence of dandruff like pseudoexfoliative material (PEX) over different parts of the lens, pupil or cornea.[2] The pathogenesis of the disease still remains unknown with multiple factors including genetic, environmental or diet factors being considered to be responsible for PEX formation.[3]

Ritch and Schlötzer-Schrehardt observed that the lens capsular deposits characteristically show a three ring (3R) pattern. The central disk may be absent in 20 % – 60 % of cases. An early (precapsular) stage is represented by the presence of a homogenous ground glass appearance of the lens surface in one eye compared to the other. At a later (pregranular) stage there is a characteristic ring of about 80 faint, radial, nongranular striae which may appear on the mid-third of the anterior capsule lying posterior to the iris. Ultrastructurally, microfibrils form the crux of the precapsular layer.[4] However, Amritha et al. described four patterns of PXF deposits on anterior lens capsules such as classic 3R, two ring (2R), radial pigmentary (RP), and combined (CR).[5]

The two most important risk factors for surgical complications in a patient of cataract with PEX include zonular weakness and poor pupillary dilatation. Usually, the eyes having cataract with PEX pose a greater risk for posterior capsule tear / rent, zonular dialysis, vitreous loss, and dropped nucleus or fragment during intraoperative period. Such patients postoperatively have a higher chance of inflammation in the form of increased aqueous flare and cells, fibrin reaction, posterior capsule opacification, posterior synechiae, anterior capsule phimosis, and delayed intraocular lens decentration and dislocation. The extra ocular tissues that are implicated in PEX include lung, skin, liver, heart, kidney, gallbladder, blood vessels, extraocular muscles, connective tissue in the orbit and meninges.[4]

Due to the anterior movement of the iris – lens diaphragm with associated zonular weakness the anterior chamber angle is often narrow. Often the pupil dilates poorly. Zonular weakness results in phacodonesis and iridodonesis which ultimately predispose to zonular dehiscence, vitreous loss and lens dislocation pre- and post-cataract surgery.[6]

Zonular weakness resulting in poor zonular support to the lens and posterior chamber intraocular lenses needs to be taken into consideration during the pre- and post-operative management of patients with PEX undergoing cataract surgery.[6] Often the reduced endothelial cell count explains the diffuse corneal endothelial decompensation.[7,8] There is an increased incidence of bullous keratopathy associated with PEX endotheliopathy.[8] Decreased endothelial cell density along with increased pleomorphism and polymegethism of the cells usually occur as a sequelae to raised intraocular pressure in eyes with PEX.[9] Care needs to be taken during surgery as the corneal endothelium in eyes with PEX is highly vulnerable to cataract surgery.[9,10,11]

Cataracts are a common occurrence in PEX patients and PEX has been found to be associated with zonular lysis intraoperatively during cataract surgery.[12,13,14] Furthermore the clinical signs that aid in early diagnosis include pigment loss from the peri-pupillary area resulting into transillumination defects, poor pupillary dilatation and pigment dispersion into the anterior chamber after mydriasis, melanin deposition over trabecular meshwork and Schwalbe's line. Also, the presence of posterior synechiae without any aetiology and the occurrence of haemorrhage in iris stroma following mydriasis also suggest pseudoexfoliation syndrome. The PEX material deposited on the weak zonular fibres can result in phacodonesis, subluxation and dislocation of lens. Open angle glaucoma occurring secondary to pseudoexfoliation is also known as glaucoma capsulare. It has a much serious clinical course and is associated with a worse prognosis than the primary open angle glaucoma. Often it requires an early surgical intervention as it does not respond to the conventional medical therapy. In few cases the forward displacement of the lens can lead to pupillary block resulting in an angle closure glaucoma.[15]

In order to minimise the complications several preoperative and intraoperative measures have been employed which include an increased awareness of pseudoexfoliation syndrome, thorough ocular evaluation on slit lamp biomicroscope following full pupillary dilatation, judicious control of intraocular pressure preoperatively, less iris handling intraoperatively, sufficient mydriasis during surgery, implantation of heparin coated intra ocular lenses and judicious use of steroids post-operatively.[16]

METHODS

This was a cross sectional descriptive study of patients with PEX who presented at a tertiary care eye centre in Latur, Maharashtra from May 2018 to April 2019. During this period, 100 patients were selected by simple random sampling and screened in the outpatient clinic.

The study was approved by the institutional ethics committee board and informed consent was obtained from all patients participating in the study.

Demographic profile of the patients viz., age, sex, detailed history were obtained by interviewing the participants and detailed ocular examination on slit lamp biomicroscope under full pupillary dilatation was performed and necessary investigations were conducted on predesigned and pretested proforma. After taking informed consent of all the eligible patients, they were subjected to detailed examination like history, general physical examination and systemic examination.

The patients were examined by using torch light examination, slit lamp examination, direct & indirect ophthalmoscopy, tonometry (indentation and non-contact tonometry (NCT) followed by Goldmann applanation in patients with raised IOP on screening with NCT), gonioscopy

to look for PXF deposition on other sites like iris, endothelium, angle and such patients were excluded from our study, a scan biometry for lens thickness and anterior chamber depth and fundus photography to assess the cup-to-disc (C / D) ratio in all the patients at the time of screening but those patients with glaucomatous disc damage and abnormal C / D ratio were excluded from our study. Preoperative assessment of weakened zonular integrity was done on the basis of history (trauma or any systemic disease) and focused slit lamp examination to identify the number of clock hours as well as the severity of the zonulopathy was done.

Cataract surgery was done on all patients by the manual SICS and vision both preoperatively and postoperatively was recorded. Refraction was done and documented. Best corrected visual acuity was noted, and it was followed-up postoperatively for 2 – 4 weeks.

RESULTS

The age-wise distribution shows that majority of the patients were from the age group between 61 - 70 years (54 %) (Table 1). Out of total cases, 64 % were males and 36 % were females (Table 1). Out of 100 patients, the range of IOP was 12.4 mm Hg to 23.1 mm Hg with an average IOP reading of 17.3 mm Hg. Those with raised IOP were managed preoperatively by use of topical beta blockers and prostaglandin analogues.

53 (53 %) cases were showing bilateral involvement of pseudoexfoliation syndrome and 47 (47 %) had unilateral involvement (Table 1). 64 patients were males, and 36 patients were females according to our study which showed a higher predisposition of PEX amongst males as compared to females.

Age Group			Laterality			Sex Wise		
Group	Frequency	Percentage		Frequency	Percentage	Sex	Frequency	Percentage
40 - 50	5	5	Bilateral	53	53	Male	64	64
51 - 60	14	14						
61 - 70	54	54	Unilateral	47	47	Female	36	36
> 70	27	27						
Total	**100**	**100**	**Total**	**100**	**100**	**Total**	**100**	**100**

Table 1. Distribution of Patients According to Age and Laterality

A total of 81 % cases had PXF material deposited on the peripheral zone and 19 % cases had PXF deposition on both peripheral zone and central zone but none of them showed involvement of only central zone. A total of 67 % cases had insufficient mydriasis (< 6 mm) and 33 % of the cases had sufficient mydriasis (> 6 mm) (Table 2).

Out of 100, only 27 cases showed a mature cataract, 66 had immature and 7 patients had hyper mature cataract. All of them, i.e., 100 % had nuclear cataracts. Cortical cataract was present along with advanced nuclear cataract but none of the patients had isolated cortical cataract.

Zone of PEX Deposition			Pupil Diameter		
Zone	Frequency	%	Pupil Diameter	Frequency	%
Central + peripheral	19	19	< 6 mm	67	67
Peripheral	81	81	> 6 mm	33	33
Total	**100**	**100**	**Total**	**100**	**100**

Table 2. Distribution of Patients According to Zone of PEX Deposition and Pupil Diameter

Pre-operative visual acuity ranged from HM +, PL + to 6 / 18 according to the type of cataract with maximum patients (41) belonging to the group having preop visual acuity of 6 / 36 (Table 3).

Pre-Op VA	Frequency	Percent
6 / 18	4	4.0
6 / 24	8	8.0
6 / 36	41	41.0
6 / 60	4	4.0
CF = 3 m	9	9.0
HM	11	11.0
PL + PR +	23	23.0
Total	**100**	**100.0**

Table 3. Distribution According to the Pre OP Visual Acuity

During cataract surgery several complications were encountered which included difficulty in nucleus delivery, endothelium touch, difficulty in capsulorhexis, posterior capsular rent and zonular dialysis. Amongst all these, difficulty in nucleus delivery accounted for the most commonly encountered intraoperative complication occurring in 39 patients followed by endothelium touch occurring in 20 of them followed by posterior capsular rupture in 18 of them followed by difficulty in capsulorhexis in 7 patients and weakened zonular integrity up to 2 - 3 clock hours in 5 patients (Table 4).

The above-mentioned complications were managed by intraoperative manipulations which include sphincterotomy which accounted for the most commonly employed technique to counter difficulty in nucleus delivery owing to insufficient mydriasis coupled with hard cataractous nucleus in majority of the patients (39). 21 patients required the use of iris retractors for insufficient mydriasis. Synechiolysis was employed in patients having posterior synechiae resulting in insufficient mydriasis. Posterior capsular rupture was managed by anterior vitrectomy. Zonular dialysis was managed by use of capsular tension ring. (Table 4)

Intra Op Complications			Intra Op Manipulations		
Complications	Frequency	Percentage	Manipulations	Frequency	Percentage
Difficulty in nucleus delivery	39	39	Anterior vitrectomy	18	18
Endothelium touch	20	20	CTR	5	5
None	11	11	None	10	10
PCR	18	18	Iris retractors	21	21
Rhexis difficulty	7	7	Sphincterotomy	39	39
Zonular dialysis	5	5	Synechiolysis	7	7
Total	**100**	**100**	**Total**	**100**	**100**

Table 4. Distribution of Data According to Intra Op Complications and the Manipulations Undertaken to Counter the Intra Op Complications

Post operatively, 20 patients out of 39 who had endothelium touch during nucleus delivery developed

corneal oedema which was successfully managed by NaCl ointment which was given post operatively.

Following table takes into consideration the correlation between the type of cataract and the incidence of PEX according to the age group, and according to our study, majority of patients irrespective of the type of cataract were belonging to age group of 61 - 70 years.

Chi-square test was applied, and the P value was found to be 0.84 which was not significant.

Age Group in Years	Type of Cataract						Total
	HMSC		IMSC		MSC		
	Frequency	Percent	Frequency	Percent	Frequency	Percent	
40 - 50	0	0.0	4	6.1	1	3.7	**5**
51 - 60	1	14.3	9	13.6	4	14.8	**14**
61 - 70	4	57.1	38	57.6	12	44.4	**54**
> 70	2	28.6	15	22.7	10	37.0	**27**
Total	**7**	**100.0**	**66**	**100.0**	**27**	**100.0**	**100**

Table 5. Statistical Analysis of Age Wise Distribution of Type of Cataract with PEX

Chi-square-2.69, P-0.84, Not significant

Following table studies the correlation between the type of cataract with PEX and the gender of the patient and on the basis of our study it has been observed that majority of the patients of PEX in both the sexes had immature senile cataract, males predominantly affected, also amongst patients having mature senile cataract males were affected more than females, however in case of hyper mature senile cataract cases females were affected more than males.

Chi square test was applied, and the P value was ground to be 0.39 which is not significant.

Gender	Type of Cataract						Total
	HMSC		IMSC		MSC		
	Frequency	Percent	Frequency	Percent	Frequency	Percent	
Male	3	42.9	42	63.6	19	70.4	**64**
Female	4	57.1	24	36.4	8	29.6	**36**
Total	**7**	**100.0**	**66**	**100.0**	**27**	**100.0**	**100**

Table 6. Statistical Analysis of Sex Wise Distribution and Type of Cataract

Chi-square-1.83, P-0.39, Not significant

Age group in years	PEX Deposition Zone				Total
	Central + Peripheral		Peripheral		
	Frequency	Percent	Frequency	Percent	
40 - 50	1	5.3	4	4.9	**5**
51 - 60	2	10.5	12	14.8	**14**
61 - 70	11	57.9	43	53.1	**54**
> 70	5	26.3	22	27.2	**27**
Total	**19**	**100.0**	**81**	**100.0**	**100**

Table 7. Statistical Analysis PEX Deposition Zone According to Age Group

Chi-square-0.27, P-0.96, Not significant

Table 7, 8, 9 study the correlation between the PEX deposition zone in cataract patients according to the different age groups, gender and according to the type of cataract.

In table 7 it has been observed that maximum patients belonged to age group of 61 - 70 yrs. irrespective of the zone of deposition of PEX material, with not much difference in proportion as the P value was not significant.

DISCUSSION

Prevalence of PEX is at a higher level in the older population. As such data on the clinical profile of pseudoexfoliation is very important due to higher percentage of general population in many parts of the world belonging to the older age group. In our study most of the patients with PEX were belonging to age group of 61 - 70 yrs., which is in line with other previously published reports.[17,18,19]

In this study, age wise distribution showed four (4 %) patients of age group 40 - 50 years, 14 (14 %) patients of age group 51 - 60 years, 54 (54 %) of age group 61 - 70 and 27 (27 %) of age group 71 - 80. The average age of patients was 66.13 years and about 81 (81 %) of patients were above 60 years of age. The pseudoexfoliation syndrome was a common occurrence between 60 to 80 years, the average age of the incidence was around 70 years. In the present study, 81 % of the patients were belonging to the age group between 60 - 80 years which was quite similar to earlier findings.[20]

Although the pseudoexfoliation syndrome starts in mid adulthood but becomes frankly manifested only in later years. Women have been affected predominantly by PEX in some studies while other studies have found equal or greater prevalence in men. In our study, male patients were predominantly affected by pseudoexfoliation as compared to females. This can be explained by the fact that our study being conducted in a rural area where males were exposed more to the sunlight (outdoor) as compared to females and exposure to sunlight is considered as a major risk factor for pseudoexfoliation syndrome. However, studies regarding the sex distribution of pseudoexfoliation syndrome were conflicting. In our study, 53 (53 %) of patients had clinical bilateral involvement of pseudoexfoliation syndrome and 47 (47 %) had unilateral involvement. This finding was similar to earlier finding.[21]

Another study comparing the frequency of unilateral versus bilateral involvement in pseudoexfoliation is not conclusive.

A finding of bilateral involvement of pseudoexfoliation syndrome in 53 % cases in the present study was quite comparable to most of the earlier studies (22 - 26). A higher prevalence rate of bilateral involvement was because it was evidenced after 5 - 10 years of unilateral clinical presence. Clinically, unilateral involvement often predisposes to bilateral involvement within 5 - 10 years after diagnosis. The most significant and consistent clinical feature was the pseudoexfoliation material at the pupillary border of which pupil being the most common site of deposition of pseudoexfoliative material followed by surface of iris which can be accounted for poor mydriasis in case of pseudoexfoliation syndrome and involvement of angle with pseudoexfoliative being late presentation.[27]

Out of 100 patients in the present study group, the range of IOP was from 12.4 mm Hg to 23.1 mm Hg with an average IOP of 100 eyes with pseudoexfoliation syndrome being 17.3 mm Hg. In patients with pseudoexfoliation syndrome, 13 (13 %) had increased IOP at the time of diagnosis. Patients who had pseudoexfoliation syndrome but not glaucoma should be considered vulnerable to glaucoma, because 15 % of such patients developed increased IOP within 10 years. Hence there is a need for a regular and careful follow up in patients who have pseudoexfoliation syndrome for glaucoma evaluation.[27]

In our study, only 33 % of the cases had sufficient mydriasis and a total of 81 % cases had PXF material deposited on the peripheral zone, and 19 % cases had PXF deposition on both peripheral zone and central zone. This may be due to usual involvement of the muscle cells in pseudoexfoliation material fiber formation.[8]

In our study, patients who had isolated cortical cataract were not included. Ritch et al. (2001) have also reported a higher prevalence of nuclear cataract in pseudoexfoliation syndrome. This was because of the increased rigidity of the iris in pseudoexfoliation syndrome occurring as a result of vascular compromise along with other changes like deposition of pseudoexfoliation material, iris atrophy and loss of iris stroma-moth eaten appearance.[4,16]

CONCLUSIONS

The results of present study indicate that pseudoexfoliation presents a series of challenges which require a thorough careful preoperative planning coupled with an excellent intraoperative care to ensure a safe surgery and a successful postoperative result. It is associated with insufficient mydriasis, phacodonesis and zonular dehiscence. Surgical modifications like sphincterotomy, anterior vitrectomy and use of capsular tension rings (CTR) improves the outcome of the surgery and also gives the better visual quality.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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