

GLAUCOMA IN PSEUDOEXFOLIATION- CLINICAL PROSPECTIVE STUDY*Balasubramanian M. Manickavelu¹, Anuradha P. Padmanabhan²*¹Senior Assistant Professor, Department of Ophthalmology, Government Tiruvannamalai Medical College and Hospital, Tiruvannamalai.²Junior Resident, Department of Ophthalmology, Government Villupuram Medical College and Hospital, Villupuram.**ABSTRACT****BACKGROUND**

Pseudoexfoliation is one of the common cause of secondary open-angle glaucoma worldwide with a mean progression rate higher than primary open-angle glaucoma. In India, prevalence rate of pseudoexfoliation is around 2% (Hiller et al). In South India, the prevalence rate is 6% in >40 years of age as per Krishnadas et al in 2003.

The aim of the study is to study the demographic aspects of pseudoexfoliation, the frequency of glaucoma in patients with pseudoexfoliation syndrome and to assess the treatment response in pseudoexfoliation syndrome.

MATERIALS AND METHODS

The study was conducted among 96 patients with pseudoexfoliation who attended OP Department of Ophthalmology, Government Tiruvannamalai Medical College and Hospital, Tiruvannamalai, from January 2017 to June 2017. Complete ocular examination with visual acuity, anterior segment examination, intraocular pressure, gonioscopy, fundus examination, central corneal thickness, visual field, ultrasound B scan and ultrasound biomicroscopy was done.

RESULTS

Incidence of glaucoma is more common in pseudoexfoliation and most of them have open angles. All patients with pseudoexfoliation should undergo complete glaucoma evaluation for early detection. Further ophthalmologist should focus on detection of pseudoexfoliation, since it is related to high risk of operative complication.

CONCLUSION

Incidence of glaucoma is more in pseudoexfoliation with most common bilateral presentation with open angles with recalcitrant intraocular pressure. Severity of optic nerve damage and with progression of field defects appeared to be more compared to primary open-angle glaucoma. Better response to combination drug therapy and surgical therapy than primary open-angle glaucoma.

KEYWORDS

Pseudoexfoliation Glaucoma, Intraocular Pressure, Visual Fields.

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BACKGROUND

Glaucoma is one of the leading causes of irreversible blindness worldwide. Pseudoexfoliation is one of the common causes of secondary open-angle glaucoma worldwide. It is noted to be a more aggressive disease with a mean progression rate higher than primary open-angle glaucoma.

Pseudoexfoliation syndrome is a systemic microfibrilopathy, which targets ocular tissues through gradual deposition of proteinaceous material.¹ This fibrillar material is produced by cells in the anterior segment in response to oxidative stress. Clumps of fibrillar material

released into extracellular spaces gets deposited into corneal endothelium, ciliary epithelium, trabecular meshwork, iris, anterior capsule of lens, zonules, anterior vitreous face and conjunctiva. Clinically, these appear as grayish white flakes. This pseudoexfoliative material gets accumulated in the trabecular meshwork and leads to elevated intraocular pressure, which leads to glaucoma.²

Systemically, this exfoliative fibrilopathy has also been reported in skin, visceral organs and associated with an increasing number of vascular disorders, sensorineural hearing loss and Alzheimer's disease.

Aim of the Study

- To study the frequency of glaucoma in patients with pseudoexfoliation syndrome.
- To study the clinical spectrum of glaucoma in pseudoexfoliation syndrome.
- To assess the treatment response in pseudoexfoliation glaucoma.

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Inclusion Criteria

1. All patients diagnosed as pseudoexfoliation syndrome with age group of 40-80 years.
2. Both males and females were included.
3. Unilateral and bilateral pseudoexfoliation cases were included.

Exclusion Criteria

1. Patients with less than 40 years of age.
2. Patient with previous history of uveitis or ocular trauma.
3. Patients with history of exposure to intense infrared lights, i.e. glassblowing.
4. Patient with known cases of POAG and angle-closure glaucoma who were on medication.

MATERIALS AND METHODS

A total of 96 patients with pseudoexfoliation who attended the outpatient Department of Ophthalmology, Government Tiruvannamalai Medical College and Hospital, Tiruvannamalai, from January 2017 to June 2017 were investigated. The study protocol was approved by the institutional ethical committee.

Demographic details of all patients were noted. Patients were subjected to detailed clinical history and complete ocular examination. Case sheet pro forma were drawn up and details of each patient were recorded.

Completed Ocular Examination Includes-

- a. Visual acuity- Visual acuity and best corrected visual acuity by Snellen’s visual acuity chart.
- b. Anterior segment examination by slit-lamp biomicroscopy and the following details were observed.
 - Conjunctiva - Circumcorneal congestion.
 - Cornea - Oedema, pseudoexfoliation material in endothelium and pigmentation.
 - Anterior chamber - Depth, aqueous flare, pseudoexfoliation materials.
 - Iris - Transillumination defects, pattern.
 - Pupil - Size, pseudoexfoliation material in papillary margin, reaction to light.
 - Lens - Exfoliation material in anterior lens surface, cataract association, triple ring sign.
- c. Intraocular pressure measured with Goldmann applanation tonometer. The values were taken after correcting the CCT.
- d. Gonioscopy- Status of angles of anterior chamber examined with Goldmann three mirror gonioscope - grading was done according to Shaffer’s criteria and presence of pseudoexfoliation material or pigmentation in angle is recorded.
- e. Detailed fundus examination- By using direct ophthalmoscopy- changes in the optic disc, cup-disc ratio, retinal nerve fibre layer damage, thinning of neuroretinal rim and shifting of retinal vessels were noted. Findings were confirmed by slit-lamp biomicroscopy with +90 dioptre lens and indirect ophthalmoscopy.

- f. Central corneal thickness- Central corneal thickness measured by using pachymetry.
- g. Visual field examination- Visual fields were assessed with automated perimeter (Octopus 301).
- h. Ultrasound B scan and ultrasound biomicroscopy in selected patients.

Complete ocular examination and measurements were done by a single person to avoid interobserver variations.

Pseudoexfoliation glaucoma was diagnosed on the basis of pseudoexfoliation material on slit-lamp examination, IOP >21 mmHg, glaucomatous cupping on fundus examination, pigmentation of trabecular meshwork on gonioscopy, glaucomatous field defects on perimetry.

OBSERVATION AND RESULTS

This study includes 96 patients with pseudoexfoliation who came to the Department of Ophthalmology, Government Tiruvannamalai Medical College and Hospital, Tiruvannamalai, from January 2017 to June 2017. Out of 96 patients, 55 patients were males and 41 patients were females.

Age in Years	Number of Cases	Percentage
41-50	6	6
51-60	34	36
61-70	47	49
71-80	9	9

Table 1. Age Distribution of 96 Patients

In this study of 96 patients, prevalence of pseudoexfoliation was higher among the age group of 61-70 years accounting for 49% (47 cases), followed by 36% (34 cases) among 51-60 years. The youngest patient found in our study was 42 years and the oldest age of the patient was 80 years.

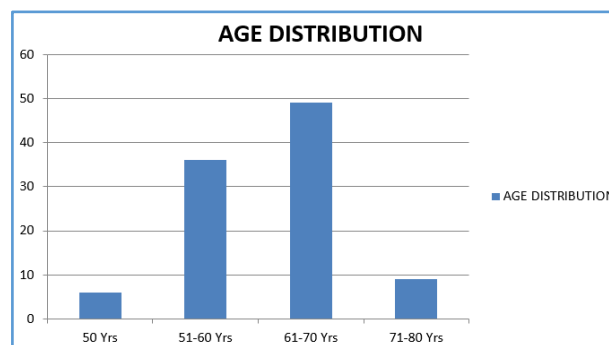


Chart 1. Age Distribution

Sex	Number of Cases	Percentage
Male	55	57
Female	41	43

Table 2. Sex Distribution

In this study of 96 patients, 55 males and 41 females were having pseudoexfoliation. There was mild male preponderance number in our study.³

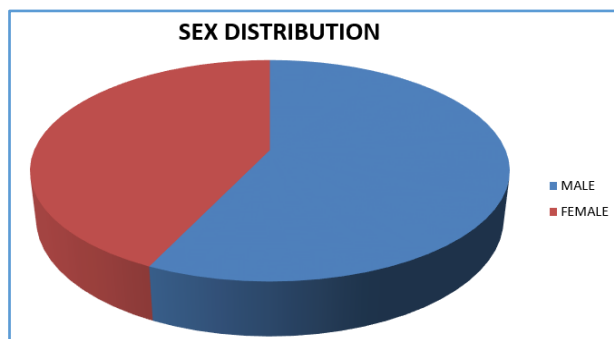


Chart 2. Sex Distribution

In this study, male preponderance to some extent explained by the fact Indian males are likely to have outdoor activities than females. Also, in our region, most of them are agricultural workers and exposure to ultraviolet exposure is high may explain the male preponderance.

Laterality	Number of Cases	Percentage
Unilateral	55	57
Bilateral	41	43

Table 3. Laterality

In this study of 96 patients, 55 (57%) were found to have unilateral pseudoexfoliation and 41 (43%) were found to have bilateral pseudoexfoliation. Unilateral pseudoexfoliation were having higher incidence than bilateral pseudoexfoliation.

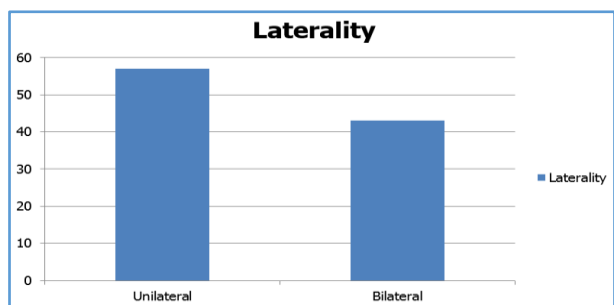


Chart 3. Laterality

In this study, 55 patients were found to be having unilateral pseudoexfoliation. They are having the risk of developing pseudoexfoliation in other eye. Hence, the unilateral pseudoexfoliation patients' need regular follow up.

Age in Years	Unilateral		Bilateral		Total	
	Number of Cases	%	Number of Cases	%	Number of Cases	%
41-50	5	9.1	1	2.4	6	6
51-60	22	40.0	12	29.3	34	36
61-70	25	45.5	22	53.7	47	49
71-80	3	5.4	6	14.6	9	9
Total	55	100	41	100	96	100

Table 4. Age and Laterality

In this study of 96 patients, both unilateral pseudoexfoliation and bilateral pseudoexfoliation were common in the age group of 61-70 years. Among the 41 patients of bilateral pseudoexfoliation, 22 patients were found in the age group of 61-70 years.

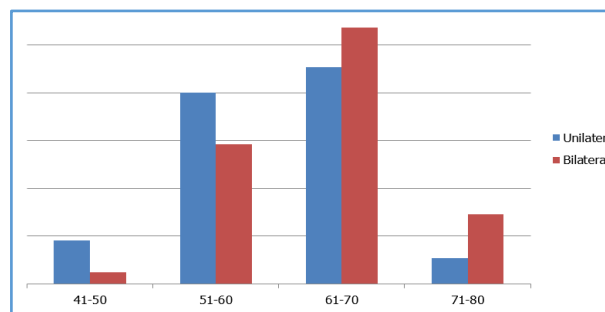


Chart 4. Age and Laterality

Among the 9 patients in the age group of 71-80 years, 6 patients had bilateral pseudoexfoliation. The percentage of bilateral pseudoexfoliation was higher in 71-80 years. This signifies that the bilateral pseudoexfoliation is common as the age increases. Hence, unilateral cases needs follow up.

Age in Years	Total Number of Pseudoexfoliation	Patients with Glaucoma		Patients without Glaucoma	
		No.	%	No.	%
41-50	6	0		6	100
51-60	34	12	35	22	65
61-70	47	19	40	28	60
71-80	9	4	44	5	56

Table 5. Glaucoma Association

In this study, out of 96 patients, glaucoma was seen in 35 patients. The incidence of glaucoma according to this study was 36%⁴ (our own study incidence).

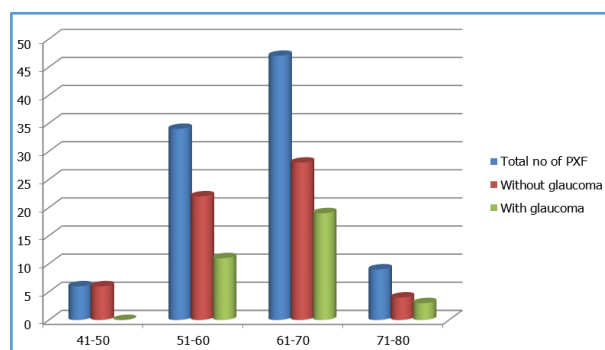


Chart 5. Age Wise Distribution of Glaucoma in Pseudoexfoliation

In this study, the incidence of glaucoma increases with age. More number of glaucoma patients are seen in the age group of 61-70 years. But, the percentage (44%) of glaucoma is common in the age group of 71-80 years.

As the age increases, the persons having pseudoexfoliation are more likely to develop glaucoma than younger ones.

IOP (mmHg)	Number of Patients	Percentage
<20	61	63.5
21-30	22	22.9
>30	13	13.6
Total	96	100

Table 6. Intraocular Pressure

In our study of 96 patients, 61 patients had an intraocular pressure less than 20 mmHg, 22 patients had an intraocular pressure 21-30 mmHg and 13 patients had an intraocular pressure more than 30 mmHg.

According to our study, the raised intraocular pressure was found in 35 patients.⁵

CD Ratio	Number of Patients	Percentage
0.3	42	43.8
0.4-0.6	30	31.2
>0.6	24	25.0
Total	96	100

Table 7. Optic Nerve Damage

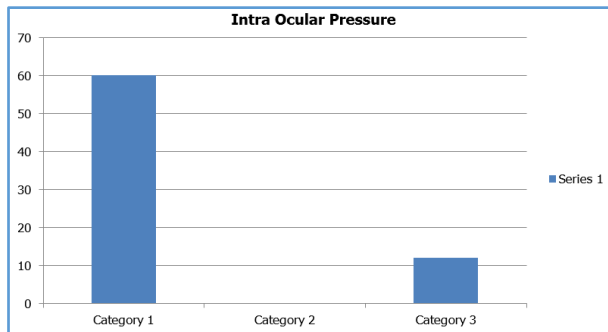


Chart 6. Intraocular Pressure

In our study of 96 patients, 42 patients had cup-disc ratio of 0.3, 30 patients had cup-disc ratio of 0.4-0.6 and 24 patients had cup-disc ratio of more than 0.6.

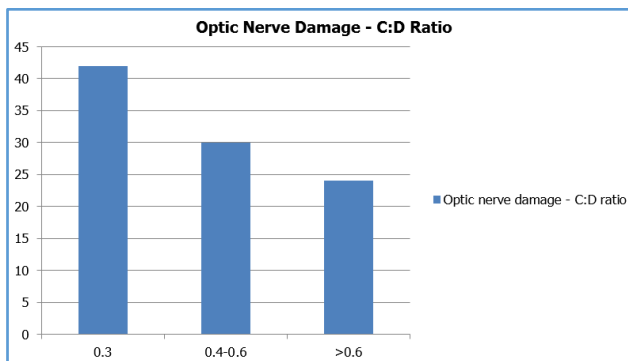


Chart 7. Optic Nerve Damage- C:D Ratio

According to our study, the severe damage to optic disc (>0.6) was seen in 25%, which is higher than the non-pseudoexfoliation patient (15%). Hence, pseudoexfoliation causes severe damage to the optic nerve and visual loss.⁶

Angle	Number of Patients	Percentage
0-1	4	4.2
2	8	8.3
3	27	28.1
4	57	59.4
Total	96	100

Table 8. Grading of Angles

In this study, 57 patients had an angle of grade IV, 27 patients had an angle of grade III, 8 patients had an angle of grade II and 4 patients had an angle of grade I.

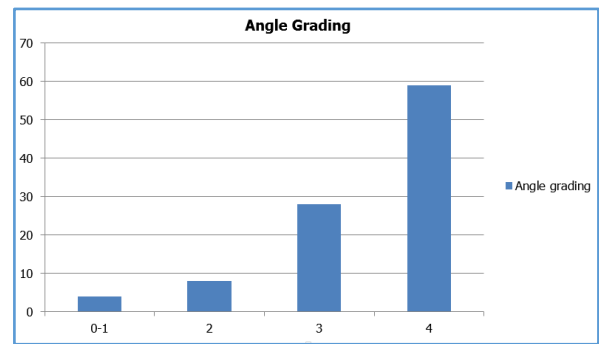


Chart 8. Angle Grading

Of these 96 patients, 12 had narrow angle (defined by Shaffer's grading as grade 0-2) and 84 patients had an open angle (defined by Shaffer's grading as grade 3-4).

Type of Glaucoma	Male		Female	
	Number	Percentage	Number	Percentage
Open angle	22	63	9	25.6
Angle closure	2	5.7	2	5.7

Table 9. Type of Glaucoma

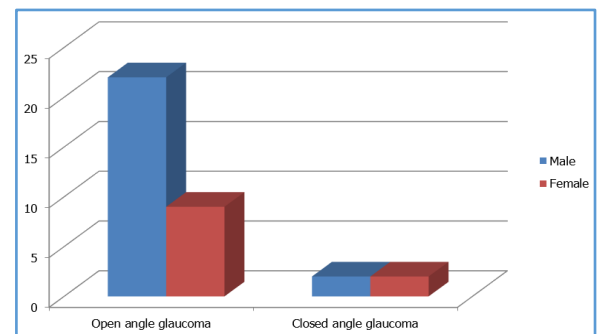


Chart 9. Type of Glaucoma

According to our study of 96 patients, 31 patients had an open-angle glaucoma and 4 patients had narrow angle glaucoma. In the 31 patients of open-angle glaucoma, 22 patients were males and 9 patients were females. Hence, pseudoexfoliation glaucoma is common among males.

Type of Glaucoma	Number of Patients
Open-angle glaucoma	31
Angle closure glaucoma	4
Angle closure suspect	8
Open angle without glaucoma	53

Table 10. Type of Glaucoma According to Angles

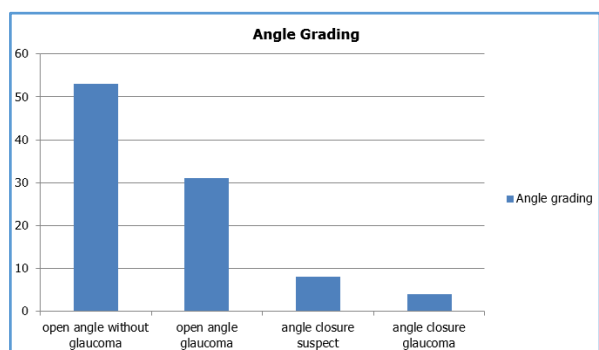


Chart 10. Type of Glaucoma According to Angles

According to our study in pseudoexfoliation syndrome, open-angle glaucoma is more common than the angle-closure glaucoma. This is explained by the mechanism of rise in IOP in pseudoexfoliation and POAG are common.⁷

	Unilateral Glaucoma	Bilateral Glaucoma	Total
Unilateral PXF	13	1	14
Bilateral PXF	9	8	17
Total	22	9	31

Table 11. Open-Angle Glaucoma and Pseudoexfoliation

Out of 22 patients with unilateral open-angle glaucoma, 13 patients had unilateral pseudoexfoliation and 9 patients had bilateral pseudoexfoliation.

In 9 patients with bilateral open-angle glaucoma, one patient had unilateral pseudoexfoliation and 8 patients had bilateral pseudoexfoliation.

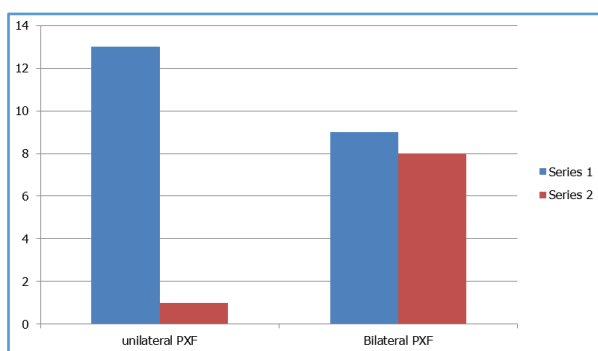


Chart 11. Open-Angle Glaucoma and Pseudoexfoliation

According to our study, 71% of patients had unilateral glaucoma and 29% had bilateral glaucoma. Hence, unilateral glaucoma is more common than bilateral glaucoma in pseudoexfoliation syndrome.⁸

Angle-Closure Glaucoma	Number of Patients
Secondary closure glaucoma	2
Primary closure glaucoma	2

Table 12. Angle Closure Glaucoma

Out of 4 patients with angle-closure glaucoma, two patients had subluxated lens. There was no trauma in these patients. Two patients had primary angle-closure glaucoma. The possible mechanism of angle closure could be pupillary block by anterior shift of iris lens diaphragm due to weakened zonules.

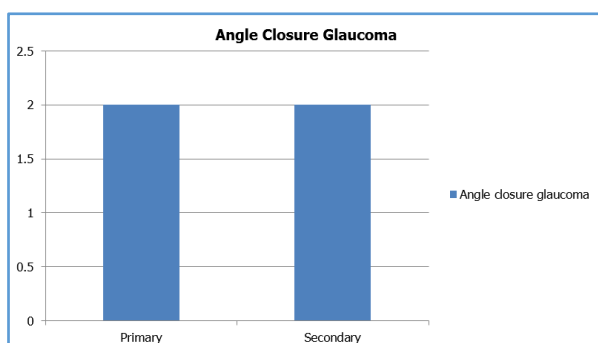


Chart 12. Angle-Closure Glaucoma

Out of 4 patients, 2 patients had bilateral pseudoexfoliation. Two patients had unilateral pseudoexfoliation with clinical features of phacodonesis and subluxation of cataractous lens producing secondary angle closure.⁹

Out of 96 patients, 53 patients had field defects. Among them, 32 patients had generalised depression, 10 patients had arcuate scotoma, 7 patients had double arcuate scotoma and 4 patients had tubular vision.

In the remaining 43 patients, fields were normal in 38 patients and not possible in 5 patients due to poor vision.

Field Defects	Number of Patients	Percentage
Generalised depression	32	33
Arcuate scotoma	10	10
Double arcuate scotoma	7	7
Tubular vision	4	4

Table 13. Field Defects

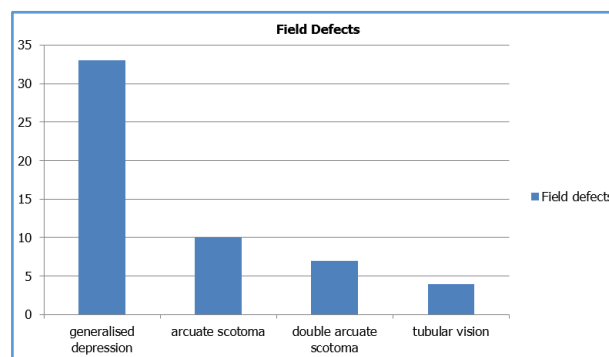


Chart 13. Field Defect

Central Corneal Thickness (CCT)	Value
Maximum CCT	0.580 mm
Minimum CCT	0.511 mm
Mean CCT	0.539 mm

Table 14. Central Corneal Thickness

In our study, mean CCT value in patients with pseudoexfoliation was 0.539 mm.¹⁰

Systemic Association- Out of 96 patients, 6 patients had diabetes mellitus, 4 patients had hypertension and 2 patients were associated with cardiovascular disease.

Treatment	Number of Patients
Medical	23
Surgical	12

Table 15. Treatment

In the study, two patients had phacodonesis treated with cataract extraction and sclera fixation IOL. During postoperative follow up, IOP is well controlled with medical treatment and glaucoma is non-progressing.¹¹

In this study, 35 glaucoma patients were started with 0.5% timolol eyedrops two times per day. At the end of 2 months, the patients were assessed regarding visual acuity,

control of intraocular pressure, glaucoma progression assessment of fields and fundus examination.

After 2 months, among the 35 patients, 7 patients (20%) had reduction in intraocular pressure and non-progression of glaucoma during follow up with single drug.¹²

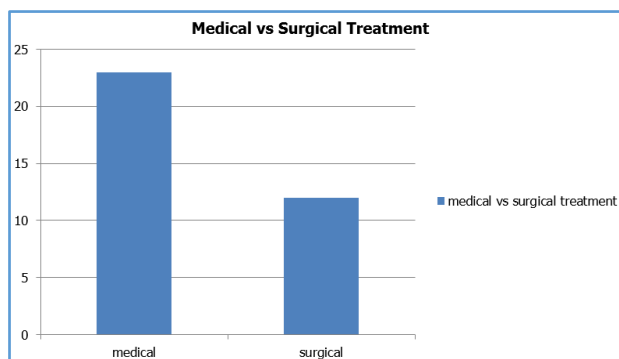


Chart 14. Medical vs. Surgical Treatment

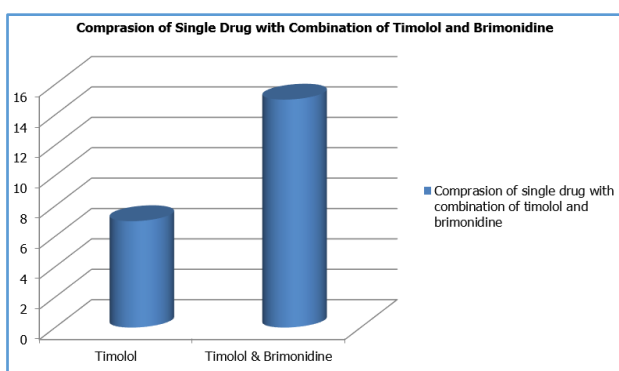


Chart 15. Comprasion of Single Drug with Combination of Timolol and Brimonidine

Rest of the 28 patients had been started with combination of 0.5% timolol and 0.2% brimonidine eyedrops. The intraocular pressure was well controlled among 16 patients (46%).

Among the 35 patients, 12 patients (34%) had poor response to medical treatment either due to poor compliance of the patient or due to poor economic status to buy medicines. In these patients, medical treatment was not sufficient to control the intraocular pressure. The intraocular pressure was controlled with filtering surgeries.¹³

In these 12 patients, combined surgery (trabeculectomy and cataract extraction with IOL implantation) was done. During the follow up period, diffuse cystic filtering bleb was formed and intraocular pressure was well controlled.

DISCUSSION

Glaucoma is the silent thief of sight, because vision loss occurs gradually over a period of time, symptoms occur only when disease is advanced, early detection is the best protection.

In this study of 96 patients with pseudoexfoliation who presented to our institute, all were subjected for detailed evaluation and analysis regarding the age at presentation, gander, laterality, glaucoma association, type of glaucoma and response to treatment.

In our study, the pseudoexfoliation syndrome is common in the age group of 61-70 years. As age increases, there is an increased incidence of pseudoexfoliation, which is comparable to Framingham study.

In our study, males were 57% and females were 43%. Clements and Luntz found higher incidence among males. In our region, most of the patients are agricultural workers and the ultraviolet light exposure is more, which may explain the higher incidence in males.

In our study, unilateral cases are having higher incidence than bilateral presentation comparable to Henry et al study. The unilateral cases have to be followed up due to possibility of becoming bilateral later in due course.

In our study, glaucoma association was found to be 36%. The incidence of glaucoma increases with age, which is similar to Lamba and Giridhar et al study.

In our study, unilateral glaucoma is more common than bilateral glaucoma. Hence, pseudoexfoliation is the commonest cause of unilateral secondary open-angle glaucoma.

In our study, the cup-disc ratio more than 0.6 was seen in 25% of patients. Hence, the optic nerve damage is more in pseudoexfoliation as compared to POAG.

In our study, 61 patients had an IOP less than 20 mmHg, 22 patients had an IOP between 21-30 mmHg and the rest of 13 patients had an intraocular pressure more than 30 mmHg.

In our study, the mean value of CCT in patients was 0.539 mm, the highest CCT was 0.580 mm and lowest was 0.511 mm, which is similar to Hepesen et al study.

In our study, angles were wide open in 59.4%. 28.1% of patients had grade 3 angle, 8.3% of them had grade 2 angles and 4.2% had closed angles.¹⁴

In our study, 60% of glaucoma patients had field defects out of which four patients had tubular vision.

In our study, out of 35 patients who have been diagnosed to have glaucoma, 23 patients responded to medical treatment and 12 patients needed surgical treatment. Out of 35 patients, 20% had control of IOP with single drug, 46% had control with combination drugs and 34% patients responded well to surgical treatment.¹⁵

Considering the poor economic status, poor compliance of the patients and average response to medical treatment, surgical treatment is one of the best in pseudoexfoliation glaucoma.

CONCLUSION

To conclude the study, it was found that the prevalence of pseudoexfoliation increases as the age advances and pseudoexfoliation is most often unilateral at the time of presentation, but eventually becomes bilateral, hence the unilateral cases needs periodic follow up.

The incidence of glaucoma is more in pseudoexfoliation and most of them have open angles.

The glaucoma is more common in bilateral pseudoexfoliation than unilateral pseudoexfoliation. The unilateral glaucoma is commoner than the bilateral glaucoma.

The intraocular pressure is having rapid rise, aggressive course and recalcitrant to treatment.

The severity of optic nerve damage is more as compared to the primary open-angle glaucoma and having advanced field defects.

The pseudoexfoliation glaucoma has better response to combination drugs as compared to single drug. The need of surgical therapy to reduce intraocular pressure is high in pseudoexfoliation glaucoma.

All patients with pseudoexfoliation should undergo complete glaucoma evaluation and early detection of glaucoma. The patients should be frequently followed up.

The intraocular pressure should be rechecked every 3-6 weeks in patients with pseudoexfoliation glaucoma. Pseudoexfoliation syndrome with no evidence of glaucoma patients should be followed every 6 months as they are having increased risk of developing glaucoma.

Pseudoexfoliation is an important cause of secondary open-angle glaucoma. It is an important cause for ocular morbidity, because of high intraocular pressure and difficult medical management, it stands out and enigmatic clinical entity. In the view of the high prevalence of glaucoma, severe damage to optic nerve increased, need of surgical therapy and high risk of operative complication related to pseudoexfoliation Ophthalmologists should focus on the detection of pseudoexfoliation.

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