



The High Prevalence of Narrow Angles and Angle Closure Glaucoma in Eyes with Exfoliation Syndrome

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To cite this article:

Sharma Ram Lal, Parmar Ranjit Singh. The High Prevalence of Narrow Angles and Angle Closure Glaucoma in Eyes with Exfoliation Syndrome. *International Journal of Ophthalmology & Visual Science*. Vol. 6, No. 1, 2021, pp. 54-58. doi: 10.11648/j.ijovs.20210601.18

Received: January 14, 2021; Accepted: January 27, 2021; Published: March 12, 2021

Abstract: *Background:* Exfoliation syndrome (ES) is characterised by deposition of flakes of fluffy material over the lens and iris, which is commonly associated with glaucoma, though in majority of the patients it is of open angle type but incidence of angle closure glaucoma is higher than general population. *Objective:* This study was aimed to establish the real association of narrow angles with exfoliation syndrome by comparing it with age related control group to rule out the confounding factor of increasing age for narrow angles. *Patients and methods:* This was a prospective study carried out among fifty patients above the age of 50 years, who were suffering from exfoliation syndrome. They were compared with another group of 50, age and sex matched patients without exfoliation. The anterior chamber angle configuration were compared between these two groups. In this study the severity of exfoliation were also studied in relation to narrowness of anterior chamber angle and severity was graded based on the extent of distribution of exfoliation. *Results:* The study found that there was a high (25%) prevalence of occludable angles (grade I, II) in patients with exfoliation syndrome as compared to control group without exfoliation (10%). Among these eyes with occludable angles, 3.2% had totally occluded angle with angle closure glaucoma. The prevalence of open angle glaucoma was (14.2%) and 3.2% eyes with ES had ocular hypertension. The prevalence of occludable angles increase with severity of exfoliation. *Conclusion* - So this study concludes that angle closure glaucoma and occludable angles are associated with ES apart from open angle glaucoma. The angle tends to be more occludable as the severity of pseudo exfoliation increases.

Keywords: Exfoliation Syndrome (ES), Pseudoexfoliation (XFS), Occludable Angle, Angle Closure Glaucoma

1. Introduction

The exfoliation syndrome (ES) previously known as pseudo exfoliation (XFS) is a widespread degenerative condition of eye, in which flakes of fluffy white material are deposited over the lens and other structures in the anterior segment of the eye. The classic pattern consists of three distinct zones that become visible when the pupil is fully dilated. Whereas this picture of exfoliation syndrome has been described, but the early stages of beginning exfoliation have not been well defined. Next to the lens, exfoliation material is most prominent at the pupillary border. Pigment loss from the iris sphincter region and its deposition on anterior chamber structures is a hallmark of ES. Despite extensive research, the exact chemical composition of exfoliation material remains unknown. Glaucoma is a common occurrence in these patients [1]; though in majority

of the patients it is of open angle type but incidence of angle closure glaucoma is higher than general population [2]. Though the association has been studied in the past but we also evaluated the relation of the severity of exfoliation to the narrowness of the angles. Hence this study was designed to find out the prevalence of narrow angle and ACG in patients with exfoliation syndrome by comparing it with age related control group to rule out the confounding factor of increasing age for narrow angles.

The exfoliation syndrome has been described more than a century ago and its most important characteristic is the greater risk of developing glaucoma [3, 4]. In a community-based study in Minnesota, 16% of all ES patients required anti-glaucoma treatment upon presentation. Of the remaining XFS patients, 44% received glaucoma therapy over the next 15 years [5]. The glaucoma onset is 2 to 3 times higher in ES with ocular hypertension than in patients with ocular

hypertension without ES [6-8]. Previous reports have shown that, in comparison with other forms of open-angle glaucoma, exfoliation glaucoma (XFG) is more resistant to medical therapy and progresses faster [9, 10]. Exfoliation glaucoma basically presents as secondary open-angle glaucoma with elevated intraocular pressure (IOP), however, due to the anterior shift of the crystalline lens as a result of zonular weakness and changes in the iris, it may also present as acute or chronic secondary angle-closure glaucoma [11]. The large magnitude of intraocular pressure (IOP) fluctuation in XFG seems to be related to its specific pathologic changes in the angle-drainage system, leading to a higher rate of transition to glaucoma and the progression of glaucoma. The XFG-associated histopathologic alterations in the outflow tissues of anterior chamber clearly differ from those observed in POAG tissues. [12]

2. Methods

This was a hospital based case control study with prospective design. A sample size of fifty patients suffering from exfoliation was taken up based upon the departmental statistics for a period of one year. The exfoliation syndrome was defined as the presence of fluffy white material on the pupillary border lens & iris on slit lamp examination prior and following dilatation of pupil. In cases where AC was shallow, pupil was dilated with short acting mydriatic (phenylephrine) followed by constriction of pupil with pilocarpine 2% before the patient left the hospital. All the patients were examined by a single person (RLS) initially and confirmed by other (RSP) to avoid observer's bias. Any patient having a disease known to affect AC angle configuration such as uveitis, previous surgery, miotic use & other secondary glaucoma were excluded from the study. Most of them were above the age of fifty years. A control group of fifty age and sex matched people were also taken. Every patient was subjected to detailed ocular examination including visual acuity, slit lamp examination, applanation tonometry and gonioscopy with Goldman 3 mirror contact lens & fundus examination. Visual fields were recorded where associated cataract was not dense. Arbitrarily severity of exfoliation was divided into three groups.

Mild - exfoliation material present at one site (pupillary border)

Moderate - material present at two sites (pupillary border

& anterior surface of lens)

Sever - material present at three sites (anterior surface of the lens)

These sites were chosen depending upon the frequency with which material is found in these eyes. The classical rings of pseudo exfoliation on anterior surface of the lens appear in late stages of the disease. Gonioscopy was done with Goldman 3 mirror contact lens that included indentation gonioscopy also. Width of angle of anterior chamber was graded according to Schaffer's classification [13]

Grade-0-No angle structure visible

Grade-I- Schwalbe line visible only

Grade-II- Grade-I+ trabecular meshwork visible

Grade-III- Grade-II + Scleral spur visible

Grade-IV- Grade-III+ Ciliary body band visible

Depending upon the angle configuration two broad groups were made, those having occludable angles (grade 0-occluded angle, grade I- potentially occludable, grade II-probably occludable) and Non occludable (grade III &IV)

Occludable angle: The angle between the posterior surface of cornea & anterior surface of iris if less than 20 degrees or when only one or two angle structure visible (grade-I, II) (scleral spur & ciliary body band)

Ocular hypertension: Any patient having IOP of more than 22 mm of Hg without any visual field defect were labeled as ocular hypertension

Glaucoma: A patient having glaucomatous cupping of the optic disc associated with visual field defects were labeled as glaucoma. The type of AC angle further subdivided them into narrow angle & open angle type. Chi square test was used for statistical analysis of the data.

3. Results

Among the fifty patients studied, there were 14 females and 36 males with male to female ratio of (2.4 to 1) and mean age of the patients was 65 years and that of controls 63 years, which was comparable. Mean intra ocular pressure (IOP) was 16 mm of Hg in the control group in both the eyes with standard deviation of 2.58 & 5.38. While mean IOP in cases was 18 & 20 mm of Hg in right and left eye respectively with standard deviation of 7.15 & 10. So the average IOP was slightly higher in case group but within normal limits of IOP. But the S.D. showed the real difference because when p-value was calculated, it was 0.02 for control and 0.008 for cases. The high standard deviation was due to the very high pressure in some of the patients with ACG.

Table 1. Mean IOP in two groups.

	Total	Mean IOP		Standard Deviation	Total.
		Right Eye	Left Eye		
Cases	50	18	18	7.15	10
Control	50	16	16	2.58	5.38
		0.02	0.008		

While 21% of the eyes with exfoliation syndrome had occludable angles (grade I, II) with potential for occlusion on indentation with gonioscope, 3.2% had occluded angle with

synechial closure in more than three quadrants of anterior chamber angle. They had associated optic disc changes and visual field defects & were labeled as angle closure glaucoma.

While in the control group the prevalence of occludable angles were only 6%, so the difference between the two groups was highly significant statistically.

Table 2. Prevalence of occludable angles in cases and control.

Angle Grade	Cases		Control	
	No. of Eyes	Percentage	No. Of Eyes	%Age
Occludable	23	25	6	6
Grade -I	13	14.1	4	4
Grade-II	7	7.5	2	2
Grade-O	3	3.2	-	-
Non Occludable	69	75		94

Table 3. Relation of AC angle depth to severity of exfoliation.

Angle	No. of Eyes with Exfoliation	No. of Eyes Without Exfoliation	Severity of Exfoliation		
			Mild	Moderate	Sever
Occludable	23	2	4	9	8
Non-Occludable	77	6	41	26	4
Total	100	8	45	35	12

There was varying degrees of cataract in 51% of the cases and 38% of the controls so refractive error was not evaluated statistically. As cataractous changes produced index ametropia in immature cataract while in mature cases it was not possible to do refraction.

Table 4. Prevalence of ocular hypertension and different types of glaucoma.

Diagnosis	Unilateral	Bilateral	Total No. of Eyes	%Age
Ocular Hypertention	3	-	3	3.2
Open Angle Glaucoma	3	5	13 (3+10)	14.1
Angle closure Glaucoma	3	-	3	3.2
No Glaucoma	9	32	73 (9+64)	79.5

Among the 92 eyes studied with exfoliation syndrome 3 eyes (3.2%) had ocular hypertension. In 13 eyes (14.2%) there was open angle glaucoma. Out of this 3 eyes had unilateral glaucoma and 5 had bilateral open angle glaucoma. All eyes having open angle glaucoma had exfoliation while 3 eyes having monocular exfoliation 1 had ACG in exfoliative eyes while contra lateral non exfoliative eyes were normal. The prevalence of angle closure glaucoma was 3.2% so total prevalence of glaucoma was 17.3%.

4. Discussion

Since its first description in 1917 by Lindberg in Finland, the exfoliation syndrome has been reported from all parts of the world. The prevalence of exfoliation increases with age [14]. The disease is of unknown etiology but HLA typing has revealed higher frequency in BW-35 patients [15].

In this study the patients included were Indian belonging to Himalayan ranges of 1000 to 3000 meter altitude. Poor vision was the commonest complaint that brought the patient to the hospital. The prevalence of ES is higher in this region (unpublished data – Shasni et al.)

In this study group exfoliation was present over the pupillary border in all cases. The second site for exfoliation was anterior lens surface. In severe cases it was present on the anterior surface of iris also. The intraocular pressure was raised in 20.5% of the eyes having exfoliation, Luntz found raised IOP in 10.1% and glaucoma in 7.1% eyes with exfoliation syndrome.[16] We also evaluated the severity of

exfoliation to the narrowness of AC angle in this study and found positive correlation between the two as 73% of eye with occludable angle has moderate to severe exfoliation. The difference between the two was highly significant.

Among the 92 eyes studied with exfoliation syndrome 3 eyes (3.2%) had ocular hypertension. In 13 eyes (14.2%) there was open angle glaucoma. Out of this 3 eyes had unilateral glaucoma and 5 had bilateral open angle glaucoma. The prevalence of angle closure glaucoma was 3.2% so total prevalence of glaucoma was 17.3%.

In this study the prevalence of occludable angle in eyes with ES was 25%, out of which 14.1% were grade-II, 7.5% grade-I and 3.2% angles were closed. In control group the prevalence of narrow angle was 6%. Laden and Schaffer [13] found narrow angles in 23% of patients with ES. Wishart et al [2] found a high incidence (25%) of narrow angles in ES, while similar were the observations of Gross et al. [17] who found 9.3% occludable angles ES patients. They had suggested multiple factors for the narrow angles including drugs used (meiotic). But in this study the severity of exfoliation was studied in a graded manner so as to relate it to the narrowness of the angle. Since the severer the disease more the chances of narrow angle glaucoma and hence the disease itself is the cause of narrow angle rather than other factors.

Herbst [18] suggested that exfoliation material produces increased pupillary block and ACG. The exfoliation material might contribute for the obstruction as 3 patients in this study having ACG, one had unilateral exfoliation and same eye had

ACG while other eye was normal.

The more important mechanism for occludable angle seems to be loose zonular apparatus as suggested by histopathological studies, [19-21] Urusula & Nauman [22] had suggested that loosening of zonule occurs as a result of impaired anchorage of zonular fibers to ciliary epithelium & lens capsule due to intercalating exfoliation material at the zonular attachments. These loose zonule shift iris lens diaphragm anteriorly which not only causes narrow angle but phacodonesis & lens displacement in some patients. The more severe the exfoliation is more the deposition of material leading to more alteration in angle configuration. The lens intumescence due to associated cataractous changes may further contribute to shallowness of the anterior chamber. Since both are the diseases of old age so can co-exist.

In order to correlate the occludability of the angle directly to the exfoliation syndrome we evaluated the angle in patients with mono ocular exfoliation. Though the numbers of patients with mono ocular exfoliation were 8 only but the significant finding in these patients was that 4 patients (50%) had occludable angles. Out of which 2 patients had occludable angles only in the eye having exfoliation. So prevalence of occludable angle were 25% in the same eye with monocular exfoliation; thereby directly correlating it with the occludability of the angle.

The prevalence of ACG in our study was 3.2% in patients with ES which is ten times higher than the prevalence reported in general population 0.1% to 0.3%. [5] But it is comparable to the prevalence reported in ES patients by Graddle & Sugar [23] (2.6%) Ross AA [24], Tarkhanen A [25], and Laden & Schaffer (4%).

Some of the factors responsible for narrow angles could be evaluated further such as AC depth & ocular biometry, which could rule out the size differences in these eyes since it was not the part of our study. But it is the combination of various lens factors that produce shallow chamber and subsequent ACG [26] Severity of exfoliation determine the occludability of the angle; if the exfoliation is more severe the chances of narrow angles & ACG are more. The presence of XFS should alert the physician to the increased risks of intraocular surgery, most commonly zonular dehiscence, capsular rupture, and vitreous loss during cataract extraction. So awareness of this condition and its associated clinical signs are important in the detection and management of glaucoma, and preoperative determination of those patients at increased risk for surgical complications.

5. Conclusion

The study found high incidence of occludable angles (21%) and angle closure glaucoma (3.2%) in eyes with exfoliation syndrome as compared to control group without exfoliation where the incidence was (10%). The prevalence of occludable angles increase with severity of exfoliation. So this study concludes that it is not only the open angle glaucoma that is common in ES but angle closure glaucoma and occludable angles are frequently seen in these patients.

The angle tends to be more occludable as the severity of pseudo exfoliation increases. The prevalence of ACG in patients with ES is many times higher than the prevalence reported in general population.

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