

Systemic associations and prevalence of exfoliation syndrome in patients scheduled for cataract surgery

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PURPOSE. To study the frequency of exfoliation syndrome (XFS) and its association with intraocular pressure (IOP) and systemic diseases in patients with age-related cataract scheduled for surgery. **METHODS.** All 1480 cataract patients had a comprehensive systemic and eye examination, including slit-lamp biomicroscopy before and after mydriasis, IOP measurement, gonioscopy, and fundus examination.

RESULTS. The percentage of XFS among patients scheduled for cataract surgery was 16.4, with no gender difference ($p=0.833$). The mean age of XFS patients (74.3 ± 7.0 years) was significantly higher when compared to the ones without XFS (66.5 ± 10.9 years) ($p<0.001$). XFS was unilateral in 41.3% of the subjects and bilateral in 58.7%. The number of subjects with XFS increased significantly with aging ($p<0.001$) (OR=1.093, 95% CI=1.073-1.14) ($p<0.001$). The most common type of cataract was nuclear in the XFS group (33.5%) and 24.6% of patients with mature cataract had XFS. In the XFS group, 11.2% of the subjects had glaucoma, which was statistically higher than the non-XFS group (4.6%) ($p<0.001$) (OR=2.67, 95% CI=1.65-4.32). Eighty-four patients had glaucoma and 27 of them (32.1%) had exfoliative glaucoma. The only systemic disease that was found to be associated with XFS was coronary heart disease with an OR of 1.49 (95% CI=1.068-2.072) ($p=0.019$).

CONCLUSIONS. XFS is a common problem in the aging cataract population of Turkey and increased IOP, glaucomatous optic neuropathy, and coronary heart disease occur more frequently in patients with XFS compared with subjects without XFS. (*Eur J Ophthalmol* 2008; 18: 551-5)

KEY WORDS. Cataract, Coronary heart disease, Exfoliation syndrome, Glaucoma

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INTRODUCTION

Exfoliation syndrome (XFS) is an age-related disorder, characterized by the production and progressive accumulation of an abnormal, extracellular fibrillar material in many ocular tissues and has important eye manifestations, including development of open- and closed-angle glaucoma and cataract with zonular instability (1-5). XFS is a systemic disorder, since exfoliation material has also been identified in skin and connective tissue portions of various visceral organs (6, 7). Previous studies have found

a relationship between XFS and vascular disorders, such as hypertension, coronary heart disease, stroke, and abdominal aortic aneurysm (8-11).

Although XFS has a worldwide distribution, the prevalence rates vary widely in different geographic locations (12, 13). The occurrence of XFS is strongly associated with age, with most cases occurring in the late 60s and early 70s. In this study our aim was to investigate several clinical aspects of XFS, such as its frequency, association with intraocular pressure (IOP), cataract type, and systemic diseases in a Turkish population of patients who

were scheduled for cataract surgery and located in the central region of Turkey.

METHODS

The study protocol was in adherence to the tenets of the Declaration of Helsinki with institutional review board approval. We included 1480 consecutive patients who were admitted for cataract surgery between 1999 and 2006 in the Department of Ophthalmology, Hacettepe University School of Medicine. Secondary cataracts related to trauma, uveitis and steroid use, congenital cataracts, and patients younger than 40 years of age were excluded from the study. Data were collected on the basis of an interview with the patient and from the records of patient files. The data included age, gender, history and duration of any eye and systemic disease, and use of ocular or systemic medications. All of the patients were examined pre-operatively by an internist.

All patients had a comprehensive eye examination including visual acuity testing, refractive work-up, slit-lamp biomicroscopy before and after mydriasis, IOP measurement with Goldmann applanation tonometry, and fundus examination. Clinical diagnosis of XFS was made by the presence of typical exfoliation material on the anterior capsule surface and the pupillary margin. Other diagnostic features included endothelial pigmentation, loss of pupillary ruff, moth-eaten iris transillumination, Sampaolesi line, and pigment deposition in the trabecular meshwork. Type of cataract was classified as nuclear, cortical, subcapsular, and mature based on slit-lamp biomicroscopy. In cases with mixed types of cataract, the predominant morphology was used in classification. Gonioscopy was performed in all eyes with XFS and eyes with an IOP >21 mmHg and established glaucoma. Criteria used to diagnose exfoliative glaucoma (XFG) were diagnosis of XFS with evidence of optic nerve head (ONH) damage and/or visual field defects, with glaucoma hemifield test as abnormal and PSD probability <0.5%. SPSS 11.50 for Windows was used for statistical analysis. Chi-square test was used to compare the frequency of XFS in different age groups and its association with the cataract type, glaucoma/ocular hypertension, and systemic disorders. A *p* value <0.05 was considered statistically significant. Multivariate, age-adjusted logistic regression analysis was done to evaluate the association of XFS and systemic associations.

RESULTS

There were 700 men (47.3%) and 780 women (52.7%) in the study group. The mean age of women was 69.3±10.4 years and men was 66.1±10.9 years (*p*<0.001). The percentage of XFS among patients scheduled for cataract surgery was 16.4 (242 patients out of 1480). The mean age of XFS patients (74.3±7.0 years) was significantly higher when compared with subjects without XFS (66.5±10.9 years) (*p*<0.001). The distribution of the patients according to the age groups and gender is given in Table I. There was a statistically significant increase in the number of XFS subjects with aging (*p*<0.001) (odds ratio [OR]=1.093, 95% confidence interval [CI]=1.073–1.14) (*p*<0.001). There was no difference in the prevalence of XFS between men (16.6%) and women (16.2%) (*p*=0.833) (Tab. I). XFS was unilateral in 41.3% of the subjects and bilateral in 58.7%. All subjects within 50–59 years age group had unilateral XFS, whereas 60% of subjects older than 70 years had bilateral XFS.

The most common cataract type was nuclear in the XFS group (33.5%) and posterior subcapsular cataract in the non-XFS group (35.3%) and 24.6% of patients with mature cataract had XFS.

Among 1480 cataract patients, 113 subjects (7.6%) had IOP levels >21 mmHg without glaucoma treatment. Eighty-four subjects (5.7%) had glaucomatous ONH damage and/or visual field abnormality, whereas 29 subjects (1.9%) had ocular hypertension (OHT). In the XFS group, 11.2% of the subjects had XFG and 3.7% had OHT, whereas in the non-XFS group, 4.6% of the patients had primary open-angle glaucoma and 1.6% had OHT, which was significantly different (*p*<0.001). With multifactorial regression analysis, glaucoma was more common in XFS group compared with non-XFS group with an OR of 2.67 (95% CI=1.65–4.32). Twenty-seven out of 84 glaucoma patients (32.1%) had XFG. The mean age of patients with XFG (75.4±6.6 years) was significantly higher than non-XFG group (69.7±10.4 years) (*p*=0.001).

Except coronary heart disease, there was no difference in the prevalence of hypertension, diabetes mellitus, chronic obstructive lung disease, and thyroid disorders between XFS and non-XFS groups (Tab. II). Using multivariate, age-adjusted logistic regression analysis, XFS was found to be significantly associated with coronary heart disease with an OR of 1.49 (95% CI=1.068–2.072) (*p*=0.019).

TABLE I - NUMBER (%) OF PATIENTS ACCORDING TO AGE GROUPS

Gender	Age groups (yrs)					Total
	40–49	50–59	60–69	70–79	80+	
Men						
XFS absent	61 (100)	132 (97.8)	165 (86.4)	190 (75.7)	36 (58.1)	584 (83.4)
XFS present	0	3 (2.2)	26 (13.6)	61 (24.3)	26 (41.9)	116 (16.6)
Women						
XFS absent	45 (100)	93 (97.9)	175 (87.1)	261 (80.3)	80 (70.2)	654 (83.8)
XFS present	0	2 (2.1)	26 (12.9)	64 (19.7)	34 (29.8)	126 (16.2)

XFS = Exfoliation syndrome

TABLE II - ASSOCIATED SYSTEMIC DISEASES

Systemic diseases	XFS group	Non-XFS group	p values
Hypertension	133 (55)	600 (48.5)	0.065
Diabetes mellitus	47 (19)	274 (22)	0.349
Coronary heart disease	69 (28.5)	233 (18.8)	0.001
Chronic obstructive lung disease	22 (9)	113 (9)	0.077
Thyroid disorders	19 (7.8)	104 (8.4)	0.777

Values are n (%).

DISCUSSION

The prevalence rate of XFS varies widely in different geographic regions: 0.3% in Poland, 3% in France, 9% in North American Indians, 16% in Russia, 18% in Norway, and 33% in Finland (13), 16.1% in Greece (14), 18.9% in Spain (15), and 7.2% in South Turkey (16). Different prevalence rates among studies could reflect true variations arising from racial, genetic, and/or geographic differences. Some of the variability could be explained by differences in techniques of assessment (dilated or not dilated), definition of XFS, and awareness of the observer. Study design (prospective versus retrospective), sampling methods (population based, hospital based, or clinic based), population size, and age distributions in the sampled populations might also affect the results.

XFS is a disease of the aging population and cataracts occur frequently in eyes with XFS (17), which might be explained in part as a function of the advanced age in XFS patients. Reported prevalence of XFS in cataract patients vary widely in different geographic regions: 25.2% in Finland (18), 35.4% in Estonia (19), 28% in Greece (20), 39.3% in Ethiopia (21), 28.7% in Spain (15), and 17.7% in

South Turkey (16). In our study, XFS was detected in 16.4% of our cataract patients and the frequency of XFS increased from 2.2% in the 50–59 years age group to 34.1% in the group ≥ 80 years.

We did not find any difference in the prevalence rates of XFS among men and women. In the age groups of 70–79 years and 80 years and over, the prevalence rates of XFS were higher in men (24.3% and 41.9%, respectively) compared with women (19.7% and 29.8%, respectively). Whether XFS is more prevalent among men or women has been a matter of controversy. Some of the previous studies have recorded higher frequencies of XFS in females (18, 22), whereas others have shown higher frequencies in males (14, 16, 23, 24), or found no difference according to gender (15, 21).

Cataracts in eyes with XFS have a higher percentage of nuclear opacities (3, 18, 19, 25). In patients with unilateral XFS, the involved eye typically has more advanced cataract. Also, in our study, the most common cataract type was nuclear in XFS group (33.5%) and posterior subcapsular cataract in non-XFS group (35.3%).

XFS is a generally accepted risk factor for glaucoma. The reported prevalence of glaucoma and/or ocular hyperten-

sion in XFS eyes has been found to vary in different populations: 7% in the United States (22), 7.5% in India (23), 13% in Iran (24), 13.3% in Ethiopia (21), 27.8% in Estonia (19), 28.8% in Crete (14), 30% in Norway (26), 32.1% in Turkey (16), 39.5% in Greece (27), 30% in Finland (3), 61% in Finland (28), and 14.9% in our study. In persons with XFS, the risk of developing glaucoma is cumulative over time. In a prospective 10-year follow-up study, the conversion rate from XFS to glaucoma was found to be 32% (29).

XFG is the most common identifiable cause of open-angle glaucoma in the world (30). The prevalence of XFS among patients with glaucoma has been reported as 1.4% in the United States (31), 26.7% in India (23), 30.5% in Turkey (16), 50% in Finland (32), 54.5% in Estonia (19), 60% in Norway (26), 75% in Sweden (33), and 31% in our study.

XFS is a systemic disorder of the extracellular matrix and exfoliation material has been found to be deposited in many organs of the body, including the heart, liver, lung, kidneys, and meninges (6, 7). Netland et al showed a marked and widespread elastosis in the connective tissue of the lamina cribrosa in all eyes with pseudoexfoliation and glaucoma (34). As elastin is a major component of the extracellular matrix of arterioles, XFS might be associated

with vascular diseases. Preliminary information has suggested a relationship with transient ischemic attacks, stroke, heart disease, and cerebrovascular disease (8-11). In our study, coronary heart disease was found to be more common in the XFS group compared to the non-XFS group. However, no difference was detected in the prevalence of hypertension, diabetes mellitus, chronic obstructive lung disease, and thyroid disorders between the XFS and non-XFS groups.

XFS is a common problem in the aging cataract population of Turkey and increased IOP, glaucomatous optic neuropathy, and coronary heart disease occur more frequently in patients with XFS compared to people without XFS. In order to prevent potential ocular and systemic complications, patients who are candidates for cataract surgery should be meticulously screened for XFS.

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