

CARDIOVASCULAR DISEASES ASSOCIATED WITH PSEUDOEXFOLIATION SYNDROME – A PROSPECTIVE CROSS-SECTIONAL STUDY

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ABSTRACT

Objectives: In recent years, pseudoexfoliation syndrome (PXF) is recognized as a systemic disorder and as an independent risk factor for cardiovascular diseases including hypertension, angina, myocardial infarction, and stroke. We studied the prevalence of cardiovascular diseases associated in patients with PXF.

Methods: It was a prospective cross-sectional study done over a period of 2 years from January 2017 to December 2018 at the Department of Ophthalmology in Sree Balaji Medical College and Hospital. A total of 100 patients with PXF both male and female above the age of 50 were included in the study. They were given a standard questionnaire to evaluate common cyclic vomiting syndrome symptoms and a history of angina, myocardial infarction, and cerebrovascular accident was noted. All patients underwent blood pressure (BP) measurement and electrocardiogram (ECG) recording.

Results: In our study which included 100 patients with PXF there were 57 male patients and 43 female patients. Most of the patients (59%) were above 65 years of age and 36 patients were diagnosed with open-angle glaucoma. A total of 62 patients had persistently elevated BP on three different occasions. Only five patients gave a positive history of angina at some point in their lives and among them, only four patients showed demonstrable changes in ECG. One patient gave a history of myocardial infarction (two showed changes in ECG) and none of the patients had cerebrovascular accidents.

Conclusion: Our study showed that more than 60% of patients with PXF had hypertension; however, a statistically significant association with other conditions was not noted.

Keywords: Pseudoexfoliation syndrome, Arterial hypertension, Ischemic heart disease, Myocardial infarction, Glaucoma.

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INTRODUCTION

Pseudoexfoliation syndrome (PXF) is the most common cause of open-angle glaucoma. It is also associated with cataract and operative complications due to zonular instability, poor pupillary dilatation, and increased permeability of vessels [1]. The cause of pseudoexfoliation material is unknown; it may be due to the production of abnormal fibrillar material that accumulates in ocular and extraocular structures [1]. PXF is now recognized as a systemic disorder and as an independent risk factor for cardiovascular diseases including hypertension, angina, myocardial infarction, and stroke [4-6]. We studied the prevalence of cardiovascular diseases associated with PXF in patients presenting to the Outpatient Department at Sree Balaji Medical College and Hospital.

Review of literature

The blue mountains eye study done in Australia showed the association of PXF with hypertension, angina, myocardial infarction, and stroke [1,6]. In another large cross-sectional study in Japan which included 1884 patients, the prevalence of arterial hypertension was high and significantly associated with PXF [1]. French *et al.* showed that the association of PXF with cardiovascular diseases was less compared to individuals with primary open-angle glaucoma and added that the latter could be a risk factor by itself [2].

A study done by Gonen *et al.* showed a high incidence of renal artery stenosis in PXF individuals [1,7]. Schumacher *et al.* showed an association between PXF and abdominal aorta aneurysm [1,11]. Andrikopoulos *et al.* postulated that common features in the pathogenesis of both atherosclerosis and PXF such as oxidative stress and inflammation could imply that PXF and cardiovascular

disorders are related or reflect different manifestations of the same process [3].

Demir *et al.* studied the association of PXF with myocardial ischemia using Doppler echocardiography and suggested that there may be an association between PXF syndrome and subclinical myocardial ischemia [12].

Praveen *et al.* studied PXF syndrome as an independent risk factor for peripheral vascular disease using ankle-brachial pressure index and Doppler imaging of the dorsalis pedis artery and showed that patients with PXF had a significantly lower ankle-brachial index as compared with controls and that PXF is associated with and maybe a risk factor for peripheral vascular diseases [14].

Vardhan *et al.* in the "Aravind Pseudoexfoliation" study of South Indian population showed that PXF was associated with higher systolic BP and more frequent ECG abnormalities but not with high blood glucose, serum cholesterol, or serum homocysteine levels [16].

Table 1: Demographics

Total no. of patients	Male	Female	With glaucoma
100	57	43	36

Table 2: Age distribution

Total no. of patients	50-55	55-60	60-65	>65
100	None	9	32	59

Table 3: Cardiovascular association

Total no. of patients	Hypertension	Angina	Myocardial infarction	Cerebrovascular accident	ECG abnormalities
100	62 (41 male 21 female)	5 (4 male 1 female)	1 (male)	None	Ischemic heart disease-40ld MI-2

ECG: Electrocardiogram

However, in a study done by Shrum *et al.* that included 472 patients with diagnosed PXF syndrome and showed no association between ocular PXF and cardiovascular or cerebrovascular mortality [1,5]. Ercegovia *et al.* examined the association between PXF and various cardiovascular diseases such as hypertension, arrhythmias, coronary artery disease (CAD), diabetes, and cerebrovascular events and only the prevalence of arrhythmia was found to be higher in patients with PXF syndrome [19].

Emiroglu *et al.* studied the coronary angiography of patients with PXF and found no significant relationship between the presence of PXF and CAD [1,4]. Lesiewska *et al.* studied the lipids and C-reactive protein levels in PXF patients and found no significant difference with age-matched controls [8].

METHODS

It is a prospective cross-sectional study done over a period of 2 years from January 2017 to December 2018 at the Department of Ophthalmology in Sree Balaji Medical College and Hospital. A total of 100 patients with PXF both male and female above the age of 50 were included in the study. The diagnosis of PXF is based on slit-lamp observations of the typical gray-white flakes at the pupillary margin or deposits on the central area of the anterior surface of lens capsule, separated from the periphery by a clear zone. They underwent comprehensive ophthalmic evaluation including visual acuity, intraocular pressure (IOP) measurement using Goldmann applanation tonometer, anterior segment, and fundus examination. Patients with increased IOP and optic disc changes underwent gonioscopy and visual field testing.

They were given a standard questionnaire to evaluate common cyclic vomiting syndrome symptoms of chest pain, breathlessness with and without exertion, palpitations, syncope, and paroxysmal nocturnal dyspnea. A history of angina, myocardial infarction, and cerebrovascular accident was noted. All patients underwent BP measurement and ECG recording.

Ethical committee clearance was obtained before start of the study and the nature of this noninvasive study was explained to each patient and proceeded only after approval.

Inclusion criteria

All patients with PXF above 50 years of age with or without glaucoma were included in the study.

Exclusion criteria

Patients with family history of hypertension and patients with diabetes mellitus (DM), dyslipidemia, blood disorders, and smokers were excluded from the study.

RESULTS

Tables 1-3 should be published in the result column not in the review of literature.

DISCUSSION

In our study which included 100 patients with PXF 36 patients were diagnosed with open-angle glaucoma which was in accordance with the general consensus that 1/3rd of PXF patients develop glaucoma. There were 57 male patients and 43 female patients; a slight male preponderance was noted. Most of the patients (59%) were above 65 years of age which also was in accordance with the fact that PXF is an age-related fibrilopathy. The elastic microfibril hypothesis states

that it is a type of elastosis with elastic microfibrils being secreted by local ocular cells. While other studies have shown that it is related to basement membrane components and also of amyloid group. The pseudoexfoliation material has also been demonstrated in tissues throughout the body including lung, heart, liver, gall bladder, skin, kidney, and cerebral meninges [3].

In our study, 62 patients had persistently elevated BP on three different occasions. Only five patients gave a positive history of angina at some point in their lives and among them, only four patients showed demonstrable changes in ECG. One patient gave a history of myocardial infarction two showed changes in ECG and none of the patients had cerebrovascular accidents. All of which were not statistically significant. Endothelial dysfunction leading to changes in systemic and ocular blood flow, oxidative stress, elastosis, impaired autonomic regulation, and baroreflex sensitivity are some of the proposed mechanisms that may account for the high prevalence of arterial hypertension in patients with PXF syndrome [1,7,9]. Homocysteine which has an important role in cardiovascular disease was found to be elevated in plasma, aqueous, and tears of patients with PXF [1].

Atherosclerosis is the major risk factor for cardiovascular diseases and hence we excluded patients with a family history of hypertension, patients with Type 2 DM, dyslipidemia, smokers, and thrombophilic disorders from our study; however, common features in the pathogenesis of both atherosclerosis and PXF such as oxidative stress and inflammation exist which could be an association [3]. An association with renal artery stenosis and abdominal aorta aneurysm with PXF has demonstrated by studies done in the past. Diffuse fibrosis and elastosis of the tunica intima and accumulation of PXF deposits in the adventitial and subendothelial connective tissue are the most common histopathological findings noted in those patients [1,11].

CONCLUSION

As ophthalmologist, we are aware of the ocular complications of PXF and this study was done to create an awareness of the cardiovascular diseases associated with this condition. Our study showed that more than 60% of patients had hypertension; however, a statistically significant association with other conditions was not noted at present. Maybe a longer follow-up with these patients and other detailed investigations like coronary angiography, carotid Doppler studies could be done in the future and possibly more patients identified. There is a definite association with cardiovascular disease and we propose that all patients with PXF should undergo detailed cardiac evaluation.

AUTHORS' CONTRIBUTION

Dr. Vikram Chellakumar, conception, data analysis, interpretation, and drafting the article. Dr. Rashmi Priyanka, data collection. Prof. Dr. M. Balakrishnan, critical revision and final approval of the version to be published.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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