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RESEARCH ARTICLES

Pseudoexfoliation syndrome in the Çorum region and its systemic associations: a population-based study

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ABSTRACT

Aim: Pseudoexfoliation syndrome (PEX) is a form of systemic elastic microfibrillopathy that affects multiple organs. The aim of this study was to investigate the prevalence of PEX in the Çorum province of Turkey and its relationship to various clinical manifestations.

Materials and Methods: A total of 1,013 patients underwent a comprehensive ophthalmic examination. Clinical diagnosis of PEX was established based on the presence of pseudoexfoliative material on the anterior lens capsule surface or the pupillary margin during slit-lamp biomicroscopy after pupillary dilation, or during surgery. Data were obtained from medical histories and patient records, including age, sex, history of ocular and systemic diseases, and systemic medication use. The systemic conditions evaluated included diabetes mellitus (DM), systemic hypertension (HT), ischemic heart disease (IHD), cerebrovascular disease (CVD), and chronic obstructive pulmonary disease (COPD). A p-value of less than 0.05 was considered statistically significant.

Results: PEX was identified in 154 of the 1,013 patients, yielding an overall prevalence of 15.2%. The prevalence of HT ($p = 0.009$), IHD ($p < 0.001$), and CVD ($p = 0.036$) was significantly higher in patients with PEX. Although the prevalence of DM was lower and COPD was slightly higher in the PEX group, these differences were not statistically significant ($p = 0.069$ and $p = 0.472$, respectively).

Conclusion: Our study demonstrates that even within geographically similar regions, the prevalence of pseudoexfoliation varies alongside different systemic comorbidities. These findings may be fundamental for identifying patients at an increased risk of systemic disease and for potentially tailoring follow-up protocols according to regional data, thereby improving public health and clinical outcomes.

Keywords: pseudoexfoliation, hypertension, cerebrovascular disease, ischemic heart disease

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INTRODUCTION

Pseudoexfoliation syndrome (PEX) is an age-related disorder characterized by the production and progressive accumulation of abnormal eosinophilic extracellular fibrillary material within various intraocular and extraocular tissues. Pseudoexfoliation fibrils may manifest in various ocular structures, including the ciliary processes, zonules, anterior lens surface, iris, corneal endothelium, trabecular meshwork, and conjunctiva (1). The condition may present unilaterally or bilaterally with lateral asymmetry. It is hypothesized that these fibrils are produced multifocally by various intraocular cell types, such as the pre-equatorial lens epithelium, non-pigmented ciliary epithelium, trabecular endothelium, corneal endothelium, vascular endothelial cells, and nearly all cell types of the iris (2). Consequently, ocular manifestations of PEX can involve all structures of the anterior segment.

PEX deposits in the anterior segment are associated with nuclear cataract formation, zonular instability, phacodonesis, lens subluxation, pigment dispersion, open-angle glaucoma, and angle-closure glaucoma resulting from pupillary or ciliary block. Additional manifestations include peripupillary atrophy, sphincter region transillumination, poor pupillary dilation, iris rigidity, asymmetric pupil size, blood-aqueous barrier defects, pseudo-uveitis, and atypical cornea guttata (1,3). Furthermore, PEX is a significant risk factor during cataract surgery. These pathological alterations explain the increased risk of intraoperative and postoperative complications, including posterior capsule or zonular rupture, vitreous loss, anterior capsule fibrosis, intraoperative miosis, hyphema, postoperative inflammation, postoperative intraocular pressure (IOP) elevation, and corneal endothelial decompensation (1-3).

Currently, PEX is recognized as a systemic disease. PEX material has been identified in extraocular muscles, cerebral meninges, the lungs, heart, liver, kidneys, gallbladder, vessel walls, and skin. Focal accumulations have been detected in these organs, particularly within the interstitial fibrovascular portions and septa. In the heart, deposits have been localized specifically on the muscle cell surfaces (4). Previous studies have reported associations between PEX and numerous systemic conditions, including hypertension, coronary heart disease, cerebrovascular events, abdominal aortic aneurysm, Alzheimer's disease, asymptomatic myocardial dysfunction, and diabetes (5,6).

The aim of this study is to investigate the prevalence of PEX syndrome in the Çorum province of Turkey and its relationship with several clinical parameters.

MATERIALS AND METHODS

Ethics committee approval for the study was obtained from Hitit University Non-Interventional Research Ethics Committee (approval number: 2023-19, date: 01.12.2023). The study was conducted in accordance with the principles of the Declaration of Helsinki. The study cohort included 1,013 patients who underwent cataract surgery performed by a single surgeon (MBÜ) between March 2019 and July 2023 at the Hitit University Hospital Department of Ophthalmology, the primary state hospital in the region. All participants underwent a comprehensive ophthalmic examination, including best-corrected visual acuity (BCVA) measured using the Snellen chart, intraocular pressure (IOP) assessment via air-puff tonometry, slit-lamp biomicroscopy, and dilated fundoscopy. Mydriasis was induced with 1% tropicamide and 10% phenylephrine hydrochloride.

The clinical diagnosis of PEX was based on the presence of exfoliative material on the anterior capsule surface or the pupillary margin observed during slit-lamp examination after dilation or detected intraoperatively with or without the use of trypan blue. Exclusion criteria included secondary cataracts related to trauma, uveitis, or steroid use; congenital cataracts; a history of vitrectomy; age under 50 years; and cases where cataract surgery was combined with vitreoretinal surgery. Only one eye per patient (the first eye to undergo surgery in bilateral cases) was included. Cataracts were classified as nuclear, cortical, subcapsular, mixed (combinations of nuclear, cortical, and/or subcapsular), or mature/white based on slit-lamp biomicroscopy.

Data were collected from patient medical histories and electronic medical records. The variables recorded included age, sex, ocular and systemic disease history, and use of systemic medications. Specific systemic conditions assessed were diabetes mellitus, systemic hypertension, ischemic heart disease, cerebrovascular disease, and chronic obstructive pulmonary disease.

Statistical analyses

Statistical analyses were performed using SPSS software (Version 22, IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as mean ± standard deviation. Categorical variables were expressed as frequencies and percentages. The independent samples t-test was used for group comparisons of continuous data. Categorical variables were compared using the chi-square test. Multivariate analysis was conducted using binary logistic regression to identify factors independently associated with PEX. Age was included as a continuous variable, while sex was treated as a dichotomous variable. Systemic comorbidities, including diabetes mellitus, hypertension, coronary artery disease, cerebrovascular disease, and chronic obstructive pulmonary disease, were included as binary covariates. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A p-value of less than 0.05 was considered statistically significant.

RESULTS

PEX was detected in 154 of the 1,013 patients, representing an overall prevalence of 15.2%. The prevalence of PEX was 14.94% in males and 15.52% in females, showing no statistically significant difference between sexes (p = 0.798). Patients with PEX (mean age: 75.94 ± 7.39 years) were significantly older than those without PEX (mean age: 69.03 ± 8.69 years) (p < 0.001). The prevalence of PEX increased with age, ranging from 2.23% in the sixth decade to 27.01% in the ninth decade. In the fully adjusted multivariate logistic regression model, age was independently associated with PEX, with a 10% increase in odds per year (adjusted OR: 1.10, 95% CI: 1.08–1.13; p < 0.001). Sex was not associated with PEX after adjustment (adjusted OR: 1.01, 95% CI: 0.69–1.47; p = 0.98). Age-specific prevalence rates are detailed in Table 1.

IOP was significantly higher in eyes with PEX (16.02 ± 2.67 mmHg) compared to eyes without it (14.77 ± 2.44 mmHg) (p < 0.001). The BCVA of patients with PEX (0.18 ± 0.15) was significantly lower than that of patients without PEX (0.21 ± 0.15) (p = 0.006). The most common cataract type in patients with PEX was nuclear (53.2%), followed by mixed (37.7%). In patients without PEX, the most frequent types were nuclear (42.1%) and mixed (41%). Demographic characteristics are presented in Table 2.

The prevalence of hypertension (p = 0.009), ischemic heart disease (p < 0.001), and cerebrovascular disease (p = 0.036) was significantly higher in patients with PEX. The prevalence of diabetes mellitus was lower and COPD was slightly higher in the PEX group, though these differences lacked statistical significance (p = 0.069 and p = 0.472, respectively). In the multivariate model, coronary artery disease remained independently associated with PEX (adjusted OR: 1.97, 95% CI: 1.33–2.92; p < 0.001). Hypertension, cerebrovascular disease, and COPD were not significantly associated with PEX in the adjusted model (p = 0.19, p = 0.09, and p = 0.99, respectively). Systemic associations are summarized in Table 3.

Table 1. Prevalence of pseudoexfoliation syndrome according to different age groups

Age (years)	PEX (n=154)	No-PEX(n=859)	Total (n= 1013)	% of PEX
50-59	3	128	131	2.23
60-69	34	285	319	10.65
70-79	77	335	412	18.69
80-89	37	100	137	27.01
≥ 90	3	11	14	21.42

PEX: Pseudoexfoliation syndrome.

Table 2. Demographic characteristics of patients with senile cataract and distribution of cataract types

	PEX + (n = 154)	PEX - (n = 859)	Total (n = 1013)	P
Age	75.94±7.39	69.03±8.69	70.08±8.86	<0.001[a]
Gender				
Male	82 (53.2%)	467 (54.4%)	549 (54.2%)	
Female	72 (46.8%)	392 (45.6%)	464 (45.8%)	0.798[b]
BCVA	0.18±0.15	0.21±0.15	0.21±0.15	0.006[a]
IOP	16.02±2.67	14.77±2.44	14.96±2.52	<0.001[a]
Type of cataract				
Nuclear	82 (53.2%)	362 (42.1%)	444 (43.8%)	
Cortical	2 (1.3%)	33 (3.8%)	35 (3.5%)	
Posterior subcapsular	0 (0%)	50 (5.8%)	50 (4.9%)	
Mixed	58 (37.7%)	352 (41%)	410 (40.5%)	
Mature/white	12 (7.8%)	62 (7.2%)	74 (7.3%)	
Total	154 (100%)	859 (100%)	1013 (100%)	

PEX: Pseudoexfoliation syndrome, BCVA: Best corrected visual acuity, IOP: Intraocular pressure, [a]: Independent samples t-test, [b]: Chi-square test

Table 3. Associated systemic diseases in patients with pseudoexfoliation syndrome

Systemic disease	PEX	No-PEX	Total	p[a]
Diabetes mellitus	38 (24.7%)	274 (31.9%)	312 (30.8%)	0.069
Hypertension	99 (64.3%)	455 (53%)	554 (54.7%)	0.009
Ischemic heart disease	62 (40.3%)	210 (24.4%)	272 (26.9%)	<0.001
Cerebrovascular disease	13 (8.4%)	36 (4.2%)	49 (4.8%)	0.036
Chronic obstructive pulmonary disease	24 (15.6%)	115 (13.4%)	139 (13.7%)	0.472

PEX: Pseudoexfoliation syndrome, [a]: Chi-square test.

DISCUSSION

Pseudoexfoliation syndrome is a systemic elastic microfibrillopathy affecting multiple systems, including the ocular, cardiovascular, and musculoskeletal systems. Its prevalence is influenced by ethnicity and geography, with reported rates ranging from 3.6% to 34.2% in Europe, 1.5% to 22.1% in Asia, and 1.5% to 40% in Africa (7-9). Identification of PEX is crucial for the prevention of associated complications.

Previous Turkish studies conducted in Northwest Central Anatolia (Eskişehir), the Eastern Mediterranean (Adana), the Middle Black Sea (Tokat), Central Anatolia (Sivas), and Marmara (Istanbul) reported PEX frequencies of 5%, 7.2%, 12.2%, 10.1%, and 11%, respectively (8,10-13). In the present study from Çorum province, also located in the Middle Black Sea region, the prevalence was 15.2%. While environmental factors such as solar/ultraviolet exposure and low temperatures have been implicated in PEX pathogenesis (14), the higher prevalence in Çorum—despite its milder climate relative to Sivas and lower UV exposure compared to Adana—suggests more complex regional factors.

This study confirmed that PEX frequency increases significantly with age, consistent with previous literature (12,15). No significant sex-based differences were found, which contrasts with the male dominance reported by Kılıç et al. in a nearby province (12). This discrepancy might stem from regional variations or the

higher sample size in our study. However, our findings align with the majority of studies that found no significant correlation between sex and PEX (16-18).

Intraocular pressure was elevated in PEX eyes, an established clinical pattern (19-21). Furthermore, the association between cataracts and PEX was confirmed (22). Nuclear cataracts were the predominant type in our PEX cohort, supporting prior research indicating a strong association between nuclear opacities and exfoliative deposits (23,24).

This study demonstrated that hypertension, ischemic heart disease, and cerebrovascular diseases are significantly more prevalent in patients with PEX, which is consistent with existing literature. PEX deposits have been proposed as a substrate for atherosclerosis and thrombus formation. Polymorphisms in the lysyl oxidase-like 1 (LOXL1) gene, which is responsible for elastin cross-linking, have been identified as a major genetic risk factor (25,26,27).

Elevated levels of apolipoprotein A, homocysteine, and other cardiovascular risk factors have also been observed in PEX patients (4). It is hypothesized that an imbalance in the matrix metalloproteinase cycle leads to fibrotic matrix dysfunction and fibrillary deposition (28). A review by Bora et al. found that PEX is substantially associated with hypertension, angina, myocardial infarction, and stroke (28). This may be related to vessel wall elastosis caused by elastin cross-linking malformations. Furthermore, PEX deposits can induce vascular endothelial defects, associated with increased proinflammatory molecules and apoptotic endothelial matrix metalloproteinases (29).

Patil et al. reported coronary artery disease in 7.9% of PEX patients, cerebrovascular events in 2.6%, and hypertension in 47.4%, with cardiac anomalies correlating with PEX severity (30). Imaz Aristimuño et al. found coronary artery disease in 3.7% and stroke in 4.6% of PEX subjects (31). Citirik et al. demonstrated a significant link between PEX and coronary artery disease in patients undergoing angiography (32). Interestingly, Kılıç et al. found a significant association in a hospital-based setting but not in a population-based study within the same region (12).

A meta-analysis by Chung et al. confirmed the association between PEX and cerebrovascular events (33). Specifically, Bora et al. noted that PEX glaucoma patients had higher rates of senile dementia, cerebral atrophy, and chronic cerebral ischemia compared to patients with primary open-angle glaucoma (POAG) (28). Akarsu et al. demonstrated that pseudoexfoliation glaucoma is associated with reduced blood flow velocity and higher resistance in the middle cerebral arteries (34).

The link between PEX and systemic arterial disease involves several mechanisms. PEX is associated with a hypercoagulable state (27). Deposits in the adventitial and subendothelial connective tissues of the aortic wall lead to vessel damage and hardening (29). Intravascular aggregation of PEX material may contribute to increased vascular resistance, impaired flow, and altered parasympathetic modulation (35). Increased stiffness in the common carotid artery has also been reported (36). In a large study of 3,546 subjects, PEX was associated with increased vascular risk, including angina, hypertension, and myocardial infarction (37).

This study has limitations. Diagnosis was based on clinical findings without histopathologic confirmation, potentially leading to underdiagnosis in early cases. Systemic comorbidities were self-reported or retrieved from records, meaning disease duration and severity were not analyzed.

In conclusion, these findings underscore the importance of comprehensive systemic evaluation in PEX patients. Our study shows that even in similar regions, PEX prevalence and systemic comorbidities vary. These differences are vital for identifying high-risk individuals and tailoring follow-up care to regional needs, ultimately improving public health outcomes.

Ethical approval

This study has been approved by the Hitit University Non-Interventional Research Ethics Committee (approval date 01.12.2023, number 2023-19). Written informed consent was obtained from the participants.

Author contribution

Surgical and Medical Practices: MBÜ; Concept: MBÜ, ZEE, SC; Design: MBÜ, ZEE, SC; Data Collection or Processing: MBÜ, ZEE, SC; Analysis or Interpretation: MBÜ, ZEE, SC; Literature Search: MBÜ, ZEE; Writing: MBÜ, ZEE. All authors reviewed the results and approved the final version of the article.

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Conflict of interest

The authors declare that there is no conflict of interest.

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