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Study of vitreoretinal interface abnormalities in patients with pseudoexfoliation syndrome



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HIGHLIGHTS

Patients with pseudoexfoliation syndrome show higher rates of vitreoretinal interface abnormalities, which increase with more pseudoexfoliation syndrome severity.

ABSTRACT

Objective: Evaluating vitreoretinal interface (VRI) abnormalities in patients with pseudoexfoliation syndrome (PEX).

Methods: In this prospective cross-sectional study (case-control design), the research sample included 67 participants (80 eyes). The control group consisted of 40 participants (40 eyes) who were ophthalmic clinic attendees without PEX, and their right eyes were selected for comparison with the case group. The case group included 27 patients (40 eyes) with PEX who were examined at the ophthalmology clinic at Latakia University Hospital in Lattakia during the period 2024–2025, and who met the study's inclusion criteria. A detailed medical history was taken, including measurement of distance visual acuity and best corrected visual acuity, Amsler grid test, slit-lamp examination, fundus examination, gonioscopy, intraocular pressure measurement using a Goldman tonometer, visual field testing, and optical-coherence tomography evaluation of the VRI. PEX patients were categorized by pseudoexfoliation severity into 3 groups: mild, moderate, severe.

Results: Rate of posterior vitreous detachment (PVD), partial PVD and epiretinal membrane (ERM) were more common in PEX group, whereas absence of PVD was more common in control group, with statistically significant differences. Complete PVD was more frequent in control group, but the difference was not statistically significant. There was a statistically significant association between ERM and PVD in PEX group as ERM was observed only in eyes with PVD. There was a statistically significant association between severity of PEX and both PVD and ERM rates in PEX group with their rates increases as the severity of PEX increases.

Key words: vitreoretinal interface abnormalities, pseudoexfoliation syndrome, posterior vitreous detachment, epiretinal membrane

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INTRODUCTION

The vitreoretinal interface (VRI) plays a vital role in maintaining retinal structure and function. In pseudoexfoliation syndrome (PEX) – an age-related condition marked by the accumulation of abnormal fibrillar material in ocular tissues – emerging evidence suggests that the VRI may be involved in disease pathology. Inflammatory processes, ischemia, and collagen abnormalities are thought to contribute to both PEX and VRI alterations. While PEX is commonly linked to anterior segment complications, such as glaucoma and cataract, posterior segment involvement, particularly at the VRI, has not been sufficiently studied. VRI abnormalities may represent an underrecognized factor contributing to visual decline in PEX patients.

This study aims to evaluate the prevalence of VRI abnormalities in PEX eyes and their relationship with disease severity.

MATERIALS AND METHODS

Study design: prospective cross-sectional study (cases and controls). Duration of the study: 12 months (between 4.03.2024 and 4.03.2025). In this study the research sample included 67 patients (80 eyes) and the study was divided into 2 groups: the case group, which included (27) patients (40 eyes) with PEX from the ophthalmic clinic attendees at Latakia University Hospital in Lattakia during the period 2024–2025, and the control group included (40) age- and sex-matched healthy volunteers (40 eyes) who were ophthalmic clinic attendees without PEX, and their healthy right eyes were selected for comparison with the case group.

Inclusion criteria: patients diagnosed with PEX presenting with any ocular complaint.

Exclusion criteria: any previous ocular surgical intervention, glaucoma, corneal diseases, severe refractive errors, ocular trauma, retinal diseases (e.g. diabetic retinopathy, tears), uveitis, advanced cataract, inflammatory or collagen diseases, pathology affecting optical coherence tomography (OCT) image (e.g. drusens).

Detailed medical history was obtained, distance visual acuity and best corrected visual acuity was measured, Amsler grid test was performed, comprehensive eye examination of anterior segment was conducted using a slit lamp, subsequently, intraocular pressure was measured with a Goldman tonometer, gonioscopy, fundus examination and OCT was performed. Patients with PEX were classified into 3 subgroups according to disease severity (mild, moderate, severe), based on amount of pseudoexfoliation material on the iris surface [1] and supplemented by the degree of pharmacologic mydriasis [2]. Pupil diameter was measured 1 h after instillation of topical tropicamide and phenylephrine. The classification was defined as follows:

- mild – pseudoexfoliation material on part of the pupillary margin, with dilation >6 mm
- moderate: pseudoexfoliation material on the entire pupillary margin, with dilation of 4–6 mm
- severe: pseudoexfoliation material on the entire pupillary margin and iris surface, with poor dilation (≤4 mm).

RESULTS

In our study we have included 67 patients, 32 males and 35 females. The age range of the study participants was between 55 and 80 years. Distribution of posterior vitreous detachment is shown in table 1.

TABLE 1

Distribution of posterior vitreous detachment in case and control groups in the sample.

		Without PVD	With PVD		Total
			partial	complete	
Case	n	13	19	8	40
	%	32.5%	47.5%	20.0%	100.0%
Control	n	26	2	12	40
	%	65.0%	5%	30.0%	100.0%
Total	n	39	21	20	80
	%	48.8%	26.3%	25.0%	100.0%
p-value		0.04	0.000	0.2	

PVD – posterior vitreous detachment.

There was statistically significant difference between case and control groups regarding the rate of partial PVD, which was significantly higher in PEX group (p-value = 0.000). The rate of eyes without PVD was significantly higher in control group compared to PEX group (p-value = 0.04). Although complete PVD was more frequent in control group, difference was not statistically significant (p-value = 0.2) (tab. 1). There was statistically significant difference between case and control groups regarding the rate of ERM, which was significantly higher in PEX group (p-value = 0.002) (tab. 2).

TABLE 2

Distribution of epiretinal membrane in case and control groups in the sample.

		Without ERM	With ERM	Total	p-value
Case	n	31	9	40	0.002
	%	77.5%	22.5%	100.0%	
Control	n	40	0	40	
	%	100.0%	0.0%	100.0%	
Total	n	71	9	80	
	%	88.8%	11.2%	100.0%	

ERM – epiretinal membrane.

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There was a statistically significant association between ERM and PVD in PEX group (p-value = 0.04). Notably, ERM was observed only in eyes with partial or complete PVD, and majority of ERM cases (77.8%) were associated with partial PVD (tab. 3).

TABLE 3

Association of epiretinal membrane with posterior vitreous detachment in pseudoexfoliation syndrome group.

		Without PVD	With PVD		Total	p-value
			partial	complete		
Without ERM	n	13	12	6	31	0.04
	%	41.9%	38.7%	19.4%	100.0%	
ERM	n	0	7	2	9	
	%	0.0%	77.8%	22.2%	100.0%	
Total	n	13	19	8	40	
	%	32.5%	47.5%	20.0%	100.0%	

ERM – epiretinal membrane; PVD – posterior vitreous detachment.

There was a statistically significant association between severity of PEX and PVD rate in PEX group (p-value = 0.001) with PVD rate increases as the severity of PEX increases (tab. 4).

TABLE 4

Frequency of posterior vitreous detachment according to pseudoexfoliation syndrome severity.

Severity of PEX		Partial PVD	Complete PVD	Without PVD	Total	p-value
Mild	n	3	1	12	16	0.001
	%	18.8%	6.3%	75.0%	100.0%	
Moderate	n	5	1	0	6	
	%	83.3%	16.7%	0.0%	100.0%	
Severe	n	11	6	1	18	
	%	61.1%	33.3%	5.6%	100.0%	
Total	n	19	8	13	40	
	%	47.5%	20.0%	32.5%	100.0%	

PEX – pseudoexfoliation syndrome; PVD – posterior vitreous detachment.

There was a statistically significant association between severity of PEX and ERM rate in PEX group (p-value = 0.007) with all cases of ERM were found in severe grade of PEX (tab. 5).

TABLE 5

Frequency of epiretinal membrane according to pseudoexfoliation syndrome severity.

		Without ERM	ERM	Total	p-value
Mild	n	16	0	16	0.007
	%	100.0%	0.0%	100.0%	
Moderate	n	6	0	6	
	%	100.0%	0.0%	100.0%	
Severe	n	9	9	18	
	%	50.0%	50%	100.0%	
Total	n	31	9	40	
	%	77.5%	22.5%	100.0%	

ERM – epiretinal membrane; PEX – pseudoexfoliation syndrome.

DISCUSSION

In our study, we found that the rates of PVD and ERM was significantly higher in the case group compared to the control group, while the absence of PVD was significantly more frequent in the control group. Our study agreed with the study of Adıyeke et al. [3], and these findings can be explained by various factors, such as ischaemia, inflammation and collagen tissue defects that play roles in the aetiopathogenesis of VRI abnormalities. Similarly, elastic fiber and collagen instability, inflammation and ischaemia are important in the aetiopathogenesis of PEX, so common pathophysiological pathways were thought to lead to PEX formation and induce VRI abnormalities. Regarding partial PVD, it was significantly more common in case group compared to control group which consistent with the study of Adıyeke et al. [3] this is likely due to impaired metabolism of collagen, fibronectin and other elastic proteins. However our study differed from the study of Adıyeke et al. [3] with regard to complete PVD which was more prevalent in control group than in case group but the difference was not statistically significant. This can be due to several factors, including the smaller sample size in our study, a higher proportion of elderly participants in the Adıyeke et al. study, and different OCT device used – namely, they utilized the Spectralis OCT (Heidelberg, Germany) while we utilized HOCT-1F (Huvitz, Dongan-gu, Republic of Korea). Additionally, PEX may be associated with anomalous posterior vitreous detachment, which could hinder the full separation of the vitreous or slow its progression compared to non-PEX individuals or PEX may also alter the process of vitreous liquefaction thereby disrupting the normal mechanism of PVD development. However the lack of statistical significance in the difference in complete PVD rates between the case and control groups in our study reduces the scientific weight of this disparity. In our study there was a significantly higher prevalence of ERM in case group compared to control group which is consistent with the study of Adıyeke et al. [3] this can be explained by ischaemia and inflammation that play important roles in the development and proliferation of ERM, as ischaemia activates transcription factors. Growth factors and other

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inflammatory mediators induce retinal pigment epithelium and microglial cells to proliferate, resulting in retinal fibrocellular membrane formation. The ERM structure consists of hyalocytes, glial cells, fibrocytes and myofibroblasts, along with non-cellular components, such as fibronectin, actin and collagen types I–IV, the detection of common structures, such as collagen and fibronectin, in PEX, similar to the ERM structure, suggests that PEX affects the VRI similar to the anterior segment.

In our study, the rate of ERM in PEX eyes was 22.5%, which is higher than the rates reported by Adıyeke et al. [3] in PEX eyes (13%), contralateral unaffected eyes (3%) in unilateral PEX, and healthy control eyes (5%). Additionally comparing with study of Lee et al. [4], the rate of ERM in PEX eyes in our study was also higher than the rate of ERM in eyes with pseudoexfoliative glaucoma (21.6%) and lower than in eyes with PEX without glaucoma (25%), similarly, in another study by Lee et al. [5], the rate of ERM in our study was higher than in eyes with pseudoexfoliative glaucoma (19%), primary open-angle glaucoma (4.1%), and healthy control eyes (2.4%). Consequently, the results of our study regarding ERM rate in PEX eyes are consistent with the broader body of published literature, which demonstrate a markedly higher prevalence of ERM among patients with PEX compared to healthy controls, as well as to patients with pseudoexfoliative glaucoma and primary open-angle glaucoma. The slight differences in ERM rates among PEX eyes between our study and previous reports may be attributed to differences in sample size, severity of PEX (which was not categorized in prior studies but was classified in our study, with the severe grade being the most common), variations in the OCT devices used, exclusion of pseudoexfoliative glaucoma patients in our sample, and possible racial and geographic differences.

Our study also demonstrated a statistically significant association between PVD and ERM, as in all eyes where ERM was detected, PVD was also present. Additionally ERM was found in approximately ⅓ of eyes with PVD. Previous studies have explained the association between ERM and partial PVD by proposing a mechanism relates to dehiscences in the inner limiting membrane that occur by transient vitreoretinal traction during the PVD process, which enables the migration and proliferation of cells of glial origin on the inner retinal surface leading to ERM formation. In our study, we found that severity of pseudoexfoliation significantly affects rates of both PVD and ERM, with rates of both increasing in parallel with increasing pseudoexfoliation severity. These findings agreed with the study of Aoki et al. [1], which investigated risk factors for corneal endothelial cell loss in patients with PEX and found that severe PEX cases exhibited significantly lower endothelial cell counts, attributing this to the deposition of pseudoexfoliation material on the cornea endothelium which leads to pseudoexfoliative keratopathy, resulting in decompensation of the corneal endothelium.

CONCLUSION

PEX is associated with VRI abnormalities, with increased rate of posterior vitreous detachment and epiretinal membrane, additionally, more severe pseudoexfoliation is associated with more rates of VRI abnormalities.

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