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Measurement of Choroidal Thickness in Patients of Pseudoexfoliation Syndrome Using Spectral Domain Optical Coherence Tomography

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Pseudoexfoliation (PEX) is a disorder characterized by the progressive accumulation of fibrillary extracellular deposits in several ocular tissues including the iris, anterior chamber angle, lens capsule and zonules. Pseudoexfoliation (PEX) syndrome is known to be associated with both ocular and choroidal blood flow changes. However there are only few studies regarding the Choroidal Thickness (CT) changes in PEX.
Aim: To evaluate the choroidal thickness in eyes with pseudoexfoliation syndrome using optical coherence tomography and to compare them with healthy controls.
Materials and Methods: Macular Choroidal thickness 70 patients of pseudoexfoliation syndrome and 70 control subjects were compared in this prospective study using Cirrhus Spectral Domain OCT (Carl Zeiss). The choroidal thickness (CT) is measured perpendicularly (from the outer edge of the hyper reflective retinal pigment epithelium to the inner sclera) at the fovea, and 1.5 mm temporal, 3.0 mm temporal, 1.5 mm nasal, and 3.0 mm nasal to the fovea using SD-OCT. Complete ocular and physical examination was also done in all subjects.
Results: The mean subfoveal CT was statistically significant thinner in PEX group as compared to healthy controls (245.48±36.42 µm vs. 312.43±30.21 µm, p value=0.03 respectively).

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The mean CT 1.5mm and 3mm nasal of fovea was also statistically significant thinner in PEX group as compared to healthy controls (205.32±26.89 µm vs. 285.36±28.01µm, p value=0.02 and 145.28±38.92 µm vs. 198.56±32.21 µm, p value=0.04 respectively).
The mean CT 1.5 mm and 3 mm temporal of fovea was also thinner in PEX group as compared to healthy controls, however results did not reach any statistical significance.
Conclusion: PEX patients have thinner choroids as compared to clinically unaffected healthy individuals.

Keywords: Pseudoexfoliation syndrome; optical coherence tomography; choroidal thickness.

1. INTRODUCTION

Pseudoexfoliation (PEX) syndrome is a genetically determined and age-dependent, generalized disorder of the elastic fiber system [1,2]. PEX is the most important identifiable risk factor for open-angle glaucoma, and PEX glaucoma accounts for 25% of all open-angle glaucomas worldwide [3,4]. In this condition there is abnormal deposition of extracellular fibrillary material on many ocular and extraocular tissues, including the periphery of blood vessels [1,2]. Ocular vasculature is also affected in this condition resulting in deposition of exfoliation material in the wall of posterior ciliary arteries (PCA), short posterior ciliary arteries and vortex veins. Blood flow disturbances have also been reported in patients with PEX [5,6]. The choroidal circulation is derived primarily from the long and short PCA with some contribution from the anterior ciliary arteries [7]. Abnormal choroidal blood supply is likely to contribute to the pathogenesis of glaucomatous optic neuropathy [8]. Resistance to flow is related to the diameter of a vessel [9]; thus, choroidal thickness (CT) may be related to the blood flow in the choroid and may be an important parameter for choroidal functioning. It may also helps in detection of pseudoexfoliation glaucomatous changes.

2. MATERIALS AND METHODS

This prospective study cross sectional study included 70 eyes of 70 healthy subjects and 70 eyes of 70 PEX patients. This study was undertaken in Government medical college Srinagar J&K India in the postgraduate department of ophthalmology.

The diagnosis of PEX was made by the presence of following findings: PEX material on the lens capsule or near the pupil; transillumination defects near the pupil; increased pigmentation or PEX material at the angle, or both; An eye was considered normal if it had an IOP of <21 mm Hg, an optic disc with normal ophthalmoscopic appearance, and normal visual field test results. All participants underwent a complete ocular examination. Biomicroscopic and fundoscopic examination with a 90-dpt lens was performed, and IOP was measured using a Goldmann applanation tonometer. Ocular axial length was measured using Ultrasound US-4000 (Nidek Co., Ltd, Japan). Visual field evaluation was done using the 30-2 SITA-Standard algorithm (Humphrey Visual Field Analyser; Carl Zeiss Meditech, USA). CT was measured by Cirrhus 5000 Spectral domain OCT (Carl Zeiss Meditech, USA).

Exclusion criteria were as follows: history or evidence of any ocular disease like age-related macular degeneration, diabetic retinopathy, central serous chorioretinopathy, epiretinal membrane, and macular dystrophy; best-corrected visual acuity of less than 20/25; history of intraocular surgery, trauma, ocular inflammation; evidence of glaucoma; poor image due to cataract, refractive errors (myopia or hyperopia) >3dpt, and astigmatism >1.5 dpt.

As choroidal thickness is strongly correlated with IOP, refractive error, and axial length these parameters were recorded in both groups [10,11].

Subjects with systemic diseases or conditions were also excluded, such as diabetes mellitus, cardiovascular disease, dyslipidemia, renal failure, malignancy, autoimmune diseases, hematological diseases, chronic obstructive pulmonary disease, uncontrolled arterial hypertension, a history of transient ischemic attack or stroke, and a history of smoking as they might affect retinal thickness or CT.

2.1 Choroidal Measurement Protocol

The same experienced technician using Cirrhus SD-OCT device performed choroidal thickness measurements. The 1 line raster was used to

measure the choroidal thickness. The 1 line raster is a 6 mm line consisting of 4096 A-scans. The images were taken in the usual manner and were not inverted to bring the choroid in closer proximity to the zero delay line, as image inversion using the Cirrus software results in a low resolution, pixilated image. To be included in this study, images had to be at least 6 out of 10 in intensity and taken as close to the fovea as possible, by choosing to image the thinnest point of the macula, with the understanding that slight differences in positioning could affect the measured thicknesses. Using the Cirrus linear measurement tool, choroidal thickness was measured perpendicularly from the outer edge of the hyper reflective RPE to the inner sclera at fovea and 1500 μ m and 3000 μ m temporal and nasal from the fovea.

Choroid-sclera interface was defined as the outermost dark-to-bright boundary (Fig. 1).

In order to generate measurements equivalent to Cirrus software, the scale was set by drawing a line over a line of a known distance, adjusting the pixel aspect ratio to 0.5, and setting global measurements in microns. The area of interest was then outlined and calculated in μ m.

The local ethical committee approved the study.

All patients provided written informed consent.

2.2 Statistical Analysis

All data were analyzed using SPSS software (version 17.0; SPSS Inc., Chicago). The descriptive statistics were presented as mean±SD. The independent-samples t test was used to compare the groups. The x^2 test was used to make comparisons between the sexes. The correlation between the age or axial length and the subfoveal CT was analyzed by Pearson correlation coefficients. A P value <0.05 was considered statistically significant.

3. RESULTS

Demographic and clinical characteristics of PEX and control groups are summarized in Table 1. The mean age in PEX group was 58.06±8.5 years and 56.04±6.8 years in control group, which was statistically insignificant (p value=0.41).

Gender differences in both the groups were comparable (p value =0.56).

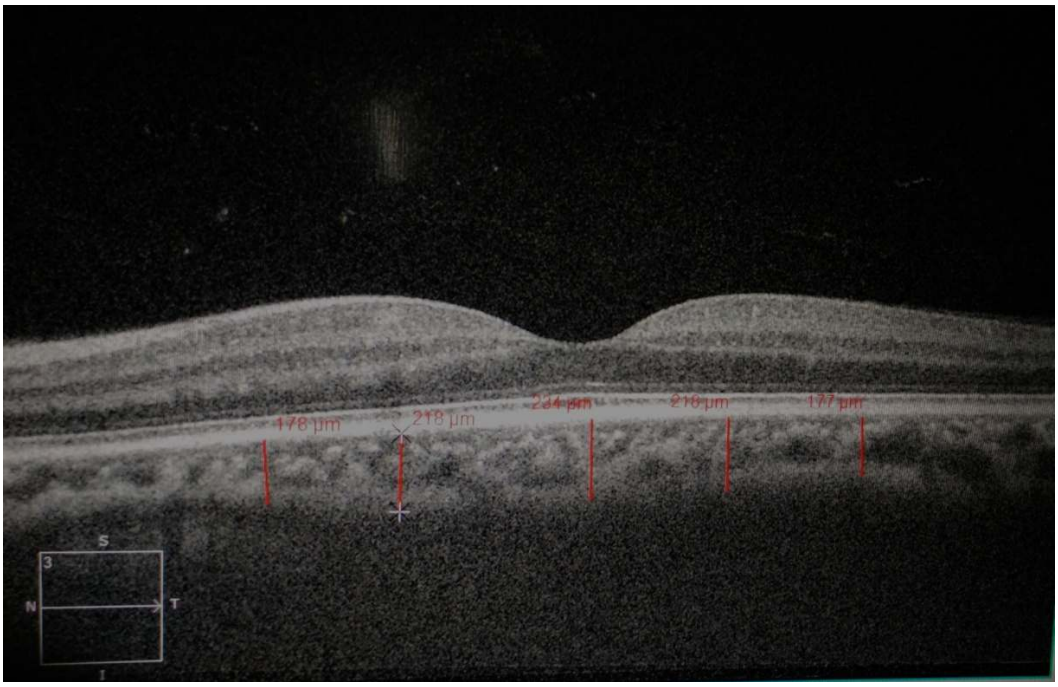

Fig. 1. Choroidal thickness measured by Cirrhus SD OCT Choroidal measurements recorded at subfoveal, 1.5 mm and 3 mm nasal to fovea and 1.5 mm and 3 mm temporal to fovea

Table 1. Patients and controls demographic data

	PEX Group n=70	Control Group n=70	P value
Age (years)	58.06±8.5	56.04±6.8	0.41
Male/Female	38/32	35/35	0.56
Mean refractive error (Spherical equivalent) Diopters	-1.5±1.1	-1.3±1.4	0.42
IOP mm Hg	14.3±2.4	14.1±3.1	0.39
Axial length (mm)	22.38±1.4	22.56±1.2	0.21

PEX= Pseudoexfoliation syndrome, IOP= Intraocular pressure, P value < 0.05 statistically significant

Table 2. Choroidal thickness measurements of pseudoexfoliation syndrome patients and controls

Measurement points	PEX Group	Controls	P value
Subfoveal CT (µm)	245.48±36.42	312.43±30.21	0.03
CT 1.5 mm nasal to fovea (µm)	205.32±26.89	285.36±28.01	0.02
CT 3 mm nasal to fovea (µm)	145.28±38.92	198.56±32.21	0.04
CT 1.5 mm temporal to fovea (µm)	230.1±29.36	245.51±32.31	0.35
CT 3 mm temporal to fovea (µm)	210.4±28.46	225.34±36.28	0.31

PEX= Pseudoexfoliation syndrome, CT = Choroidal thickness, P value < 0.05 statistically significant

Mean spherical equivalent was -1.5D±1.1 in PEX group and -1.3D±1.4 in control group, which was statistically insignificant (p value =0.42).

Intraocular pressure measurement were comparable in both groups, 14.3±2.4 mmHg in PEX group and 14.1±3.1 mmHg in control group (p value =0.39).

Axial length in PEX group was 22.38±1.4 mm and 22.56±1.2 mm in control group, which was statistically insignificant (p value =0.21).

The mean CT measurements at each location are shown in Table 2.

The mean subfoveal CT, mean CT 1.5 mm nasal to fovea and mean CT 3 mm nasal to fovea showed statistically significant thinner CT in PEX group as compared to control group.

The mean CT 1.5 mm temporal to fovea and mean CT 3 mm temporal to fovea were thinner in PEX group as compared to control group, however it was not statistically significant.

4. DISCUSSION

Pseudoexfoliation syndrome is the ocular manifestation of a systemic disease; therefore, pseudoexfoliative material deposits are not only found within orbital tissue, but can also accumulate in different part of the body like skin, lung, heart, liver, gall bladder, kidney, ear, optic nerve, blood vessels, and cerebral meninges [12,13].

Elastin constitutes a major part of the extracellular matrix of arterioles and studies have shown that there is an association of vascular elastosis with pseudoexfoliative materials. So it has been hypothesized that there is a possible association between the presence of ocular pseudoexfoliation and vascular diseases [1,2].

Choroid is a highly vascular ocular structure and it is directly affected by intraocular and perfusion pressure; therefore, real time high-definition images of the choroid are more likely to demonstrate the real time vascular status of this tissue in vivo [14]. OCT has been shown to be superior to histology to reflect accurate choroidal thickness [15]. However, exact relationship of choroidal thickness with choroidal blood flow has not been documented. Many studies have reported ocular disorders associated with altered abnormal choroidal thickness [16–19].

Therefore, a precise clinical evaluation of choroidal morphology should be important for understanding the pathogenesis of many retinal and choroidal diseases [20,21].

Spaide et al. [22] was first to describe that an 'enhanced deep imaging' (EDI) technique of OCT allows full thickness choroidal visualization. Since then, choroidal thickness has been increasingly investigated in ocular diseases, as well as in healthy eyes [23-27].

Choroidal thickness has been shown to increase in patients with Vogt–Koyanagi–Harada disease

[24] and central serous chorioretinopathy [25] or decreases in patients with pathologic myopia [10], age-related macular degeneration [20], glaucoma [26] and diabetic retinopathy [27]. These studies have hypothesized that variation in choroidal thickness may be associated with abnormality in choroidal circulation.

Dayanir et al. [28] studied the ocular blood flow changes in patients with unilateral PEX between eye clinically affected by PEX versus clinically unaffected eyes and controls. In eyes affected by pseudoexfoliation material, the ophthalmic artery experienced decreases in the peak systolic and end diastolic velocities, and increases in the resistive index compared to the control group.

Yuksel et al. [29] used color Doppler imaging to demonstrate that PEX patient had decreased peak systolic velocity in the central retinal artery, decreased end-diastolic blood flow velocities in the central retinal and short posterior ciliary arteries, and high resistive indices in the ophthalmic and central retinal arteries.

Sogawa et al. [30] found was no association between the choroidal thickness and choroidal blood flow in healthy young subjects.

However, Vance et al. [31] and Kim et al. [32] reported that sildenafil citrate increases choroidal thickness because of the vasodilatory effect of sildenafil citrate on the choroidal circulation.

Small vessels are more affected than major ones in PEX [2]. It gets accumulated in cells that regulate the local microcirculation such as, vascular endothelial cells, smooth muscle cells and pericytes [33].

So a decrease in choroidal thickness may be related to dysregulation in local choroidal microcirculation. It has been also described that accumulation of the PEX material in the vessel walls causes vascular alterations like increased permeability, obstruction, and loss of small vessels [34-36].

Sibour et al. [37] studied choroid pulsatile blood flow differences between the apparently healthy eye and the affected eye in patients with unilateral PEX syndrome.

They reported that PEX-affected eye had a flow less than that of the other eye and a mean 14% ocular blood flow reduction in the affected eye compared with its fellow.

Moreover Scullica et al. [38] found reduced carotid blood flow evaluated by echo doppler in the PEX-affected eye compared with the fellow eye.

Zengin et al. [39] reported that mean choroidal thickness was not significantly different between the PEX patients and the control cases, however PEX patients had lower mean choroidal thickness than controls, there results did not reach any statistical significance.

Turan et al. [40] study suggest that PEX is associated with an overall thinning of the subfoveal choroid which was similar to our study however major limitation of this study was measurement of CT only at the subfoveal region only.

Eroglu et al. [41] observed that clinically affected eyes of patients with PEX syndrome have significantly thinner choroids compared with the clinically unaffected eyes of patients with unilateral PEX syndrome and eyes of healthy controls, which was similar to our findings, however we had a larger series of patients.

5. CONCLUSION

Patients with clinically PEX-affected eyes tend to have thinner choroids as compared to eyes of healthy individuals, which might be a result of the altered blood flow dynamics in choroidal circulation, associated with the disease.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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