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ORIGINAL RESEARCH

Analysis of Diurnal Variation of Central Corneal Thickness in Eyes with Pseudoexfoliation Syndrome without Glaucoma and its Impact on IOP

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ABSTRACT

Background: Pseudoexfoliation syndrome (PXF) is a age related, chronic, ubiquitous abnormal accumulation of flaky fibrillary material at the anterior lens capsule, iris and pupillary margin ,corneal endothelium, angles of the eye and various other structures of the anterior segment of the eye. Substantial research has determined the effect of PXF syndrome without glaucoma on central corneal thickness (CCT).**Aim**: The aim is to determine the existence of variation in diurnal Central Corneal Thickness (CCT) and Intraocular Pressure (IOP) between eyes with Pseudoexfoliation syndrome (PXF) without glaucoma, Primary Open Angle Glaucoma(POAG) and eyes of normal patients with no existing ocular pathology and to determine its effects on the progression of the disease.**Methods:** Case control cross sectional analytical study. 63 patients with PXF without glaucoma, POAG and aged matched normal were taken. CCT and IOP measurements were taken in all patients throughout the day and variances were noted.**Results:** There was a larger variance in the CCT of the PXF group as compared to the normal population and this result was statistically significant. The variances in the POAG group and the PXF group were also similar however we could not correlate this significantly. We also analyzed the variance in CCT with IOP measurements in each group and across groups and found that PXF group had significant fluctuation in IOP when correlated with fluctuations in CCT.**Conclusion:** Patients with Pseudoexfoliation without glaucoma must undergo periodic monitoring of CCT and IOP for early detection of glaucomatous damage for prompt treatment to prevent further glaucomatous damage and progression of the disease.

Key words: Central corneal thickness, IOP, Pseudoexfoliation without glaucoma, Primary open angle glaucoma, diurnal variation

INTRODUCTION

Pseudoexfoliation syndrome (PXF) is a age related, chronic, ubiquitous abnormal accumulation of flaky fibrillary material at the anterior lens capsule, iris and pupillary margin ,corneal endothelium, angles of the eye and various other structures of the anterior segment of the eye.[1] Substantial research has determined the effect of PXF syndrome without glaucoma on central corneal thickness (CCT). [2-3] It is known that significant diurnal fluctuation of Central Corneal Thickness (CCT) and Intraocular Pressure (IOP) occurs in normal individuals with no ocular pathology.[4-5] In 2003, a study conducted by Inoue et al reported thinner central corneas in PXF (with or without glaucoma) compared to those people with no ocular pathology.[3]CCT is considered an independent risk factor of glaucoma, due to its confounding effect on the underestimation of IOP, which is also in accordance with the study done by Brandt et al in 2004. [6]CCT and IOP are greatest in the early morning with greater fluctuation happening in 3 hours of awakening and then gradually decreases as the day progresses.[7]The aim of our study was to determine the existence of variation in diurnal CCT and Intraocular Pressure between eyes with Pseudoexfoliation syndrome without glaucoma, Primary Open Angle Glaucoma(POAG) and eyes with no ocular pathology and to determine its effects on the progression of the disease.[8]

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MATERIALS AND METHODS

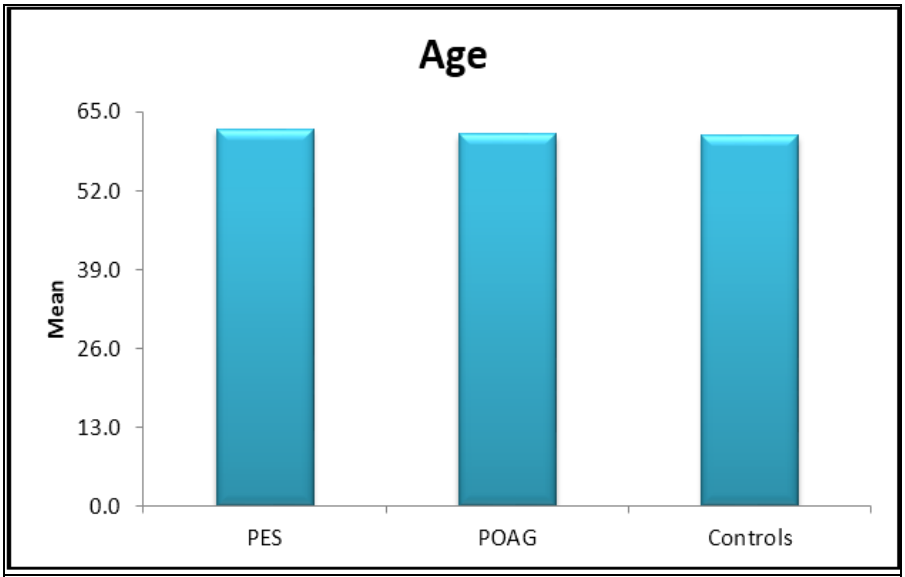
A case control cross sectional analytical study in 126 eyes of63 individuals in the age group of 50-70 years in 3 groups with 21 individuals of Pseudoexfoliation syndrome without glaucoma, 21 of Primary Open Angle Glaucoma and 21 age matched normal individualsPseudoexfoliation group patients included had characteristic flaky,granular deposits in various structures of the anterior segment including conjunctiva, cornea, iris, pupil, lens and angles of the eye on slit lamp confirmed by gonioscopic examination with normal IOP (<21 mmHg) and normal optic[9] disc (CDR ≤0.5, asymmetry ≤0.2). [9] Patients with Primary Open Angle Glaucoma had Open angles in gonioscopy with raised IOP of more than 21 mmHg with disc changes (NRR thinning, or asymmetry of 0.2 or more) and corresponding visual field changes in perimetry.[10]Normal subjects included had no ocular pathology and no evidence of glaucoma. Subjects with normal anterior segment and fundus findings except for the decrease in vision due to cataractous changes or due to refractive error were included.[9] Patients with systemic diseases like Diabetes mellitus, Pseudoexfoliation with glaucoma, History of Ocular injury, Dry eyes, Corneal Scar or hazy corneas, Keratoconus,Use of Contact lens, Post LASIK, Pseudophakia/ Aphakia, Nystagmus, Established ocular surface disorders, Subjects with refractive error of myopia or hypermetropia of >4D or astigmatism >1D were excluded from the study.[9-11] Keeping in accordance with the above inclusion and exclusion criteria, all patients were subjected to slit lamp examination of Anterior segment, Iris, Pupil, lens. Gonioscopic examination of the angle with 4 mirror sussmangonio lens ; Fundus evaluation with 78D lens in a slit lamp. IOP was measured with Goldmannapplanation tonometer under topical anaesthesia after staining the cornea with fluorescein. Goldmannapplanation tonometer is considered gold standard for IOP evaluation as it is precise and has least interobserver variability.[12]CCT was measured with Automated (TONOREF III) Pachymeter. Slit lamp examination was done to rule out corneal epithelial defects before each CCT measurement. Gonioscopic examination or pupillary dilation was avoided during the study period to prevent corneal surface damage or distortion. In accordance with the studies of similar field of research,[8,11]CCT and IOP was measured at four separate times a day at 8am, 11am, 1pm and 4pm during office hours. The times chosen are within the consulting hours of the ophthalmic clinic. Diagnoses or plan of treatment carried out is based on the clinical measures taken during this office hours. The evaluation and all the measurements were taken at all times of the day by a single observer. All parameters were analysed between the 3 groups. Informed consent was taken from the participants. Institutional Ethics committee approval was taken.

Statistical analysis

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0.(Armonk, NY: IBM Corp).To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference in the multivariate analysis the one way ANOVA with Tukey's Post-Hoc test was used.To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value 0.05 is considered as significant level.

RESULTS

A total of 126 eyes of 63 patients in 3 groups were included in this study. There was no significant difference between experiment and control groups in age and sex distribution (Graph 1 & Graph 2).



Graph 1 : Age distribution in 3 groups

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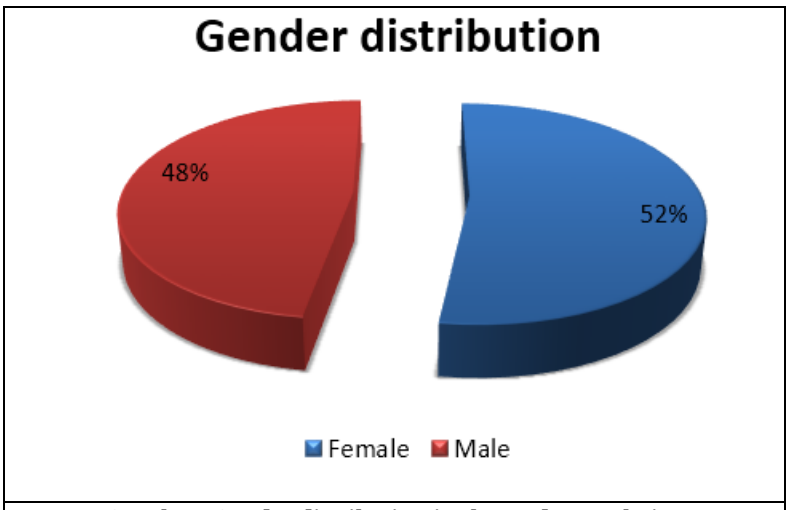

Graph 2: Gender distribution in the study population

		Mean	Significance
Pseudoexfoliation Syndrome	21	502.80	P=0.001
Primary Open Angle Glaucoma	21	503.73	
Normal patients	21	530.29	

Table 1: Comparison of CCT values in both eyes

There was statistically significant difference in CCT among patients with PXF when compared to POAG and normal subjects with p = 0.001 (Table 1)and significant variation in IOP between Pseudoexfoliation syndrome and control groups (Table 2).

		Mean	Significance
Pseudoexfoliation Syndrome	21	13.73	P=0.001
Primary Open Angle Glaucoma	21	21.72	
Normal patients	21	12.70	

Table 2: Comparison of IOP values in both eyes

		Sum ofSquares	df	MeanSquare	F	p-value
8am	BetweenGroups	14428.206	2	7214.103	26.375	.0005
11pm	BetweenGroups	24100.492	2	12050.246	46.452	.0005
1pm	BetweenGroups	23755.762	2	11877.881	46.852	.0005
4pm	BetweenGroups	20418.111	2	10209.056	39.151	.0005

Table 3 : Anova of CCT of both eyes

		Sum ofSquares	df	MeanSquare	F	p-value
8am	BetweenGroups	2711.048	2	1355.524	201.898	.0005
11pm	BetweenGroups	2011.286	2	1005.643	135.864	.0005
1pm	BetweenGroups	1995.111	2	997.556	128.590	.0005
4pm	BetweenGroups	1567.730	2	783.865	102.596	.0005

Table 4 : ANOVA of IOP of both eyes

The variation in IOP exhibited a statistically significant (P < 0.001) positive correlation with variation in CCT in Pseudoexfoliation group.

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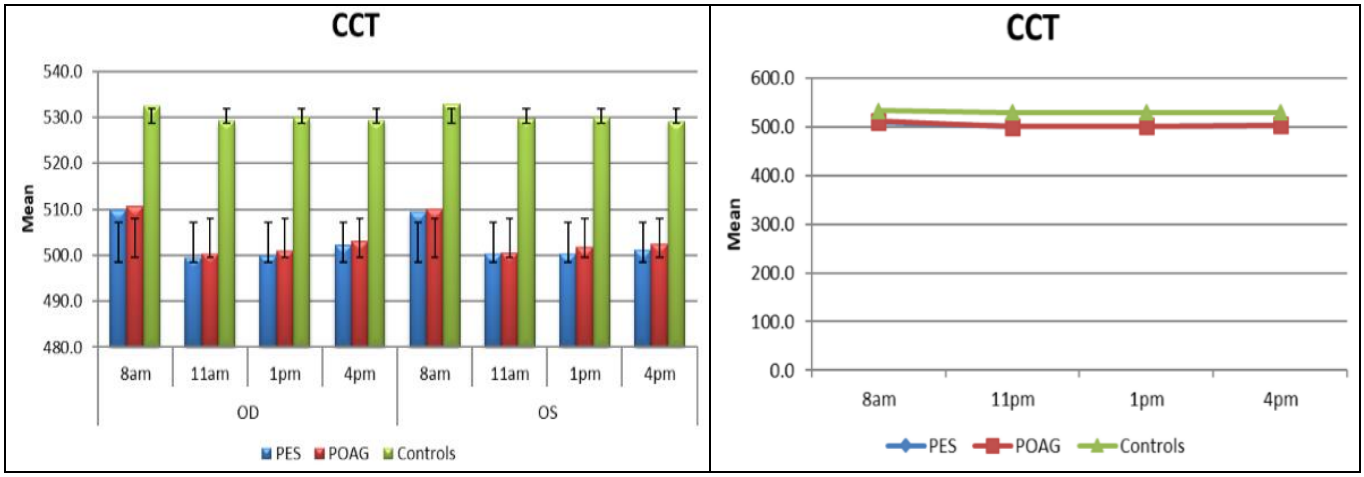
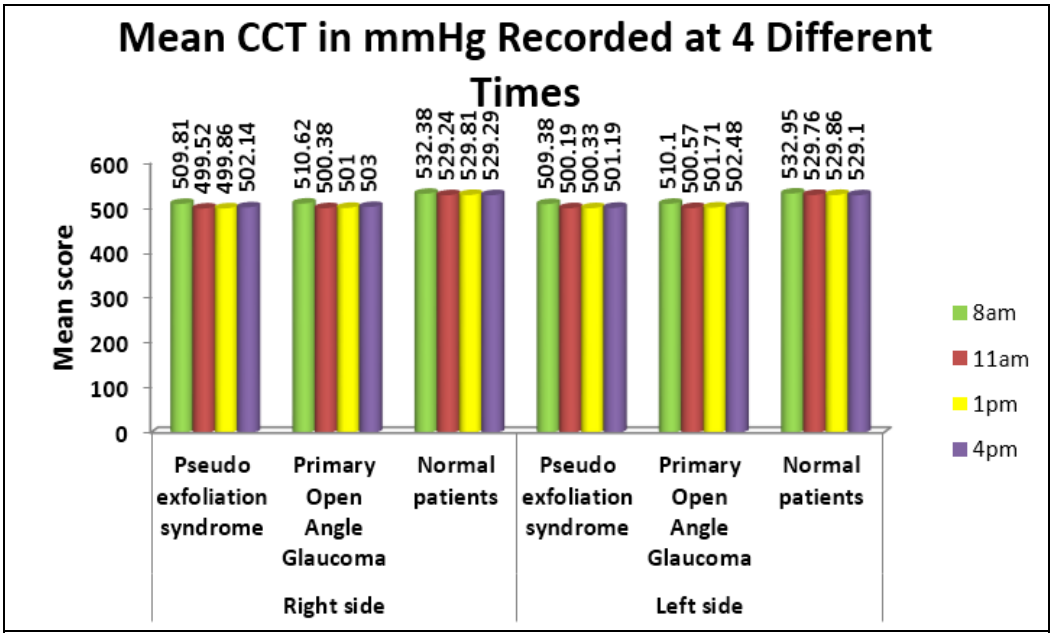
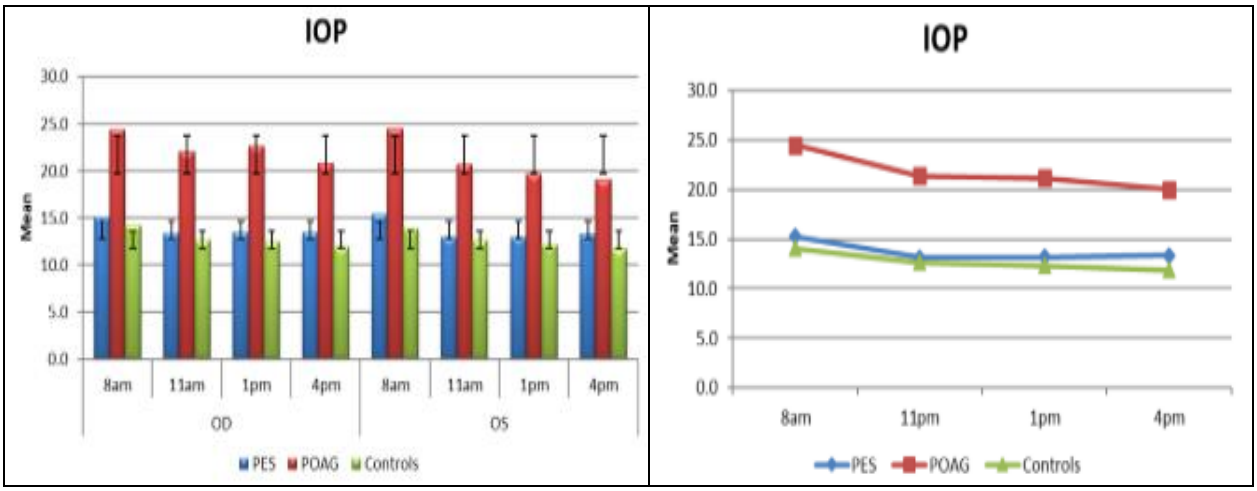




Graph 3: Comparision of CCT among 3 groups in both eyes at 4 different times of the day



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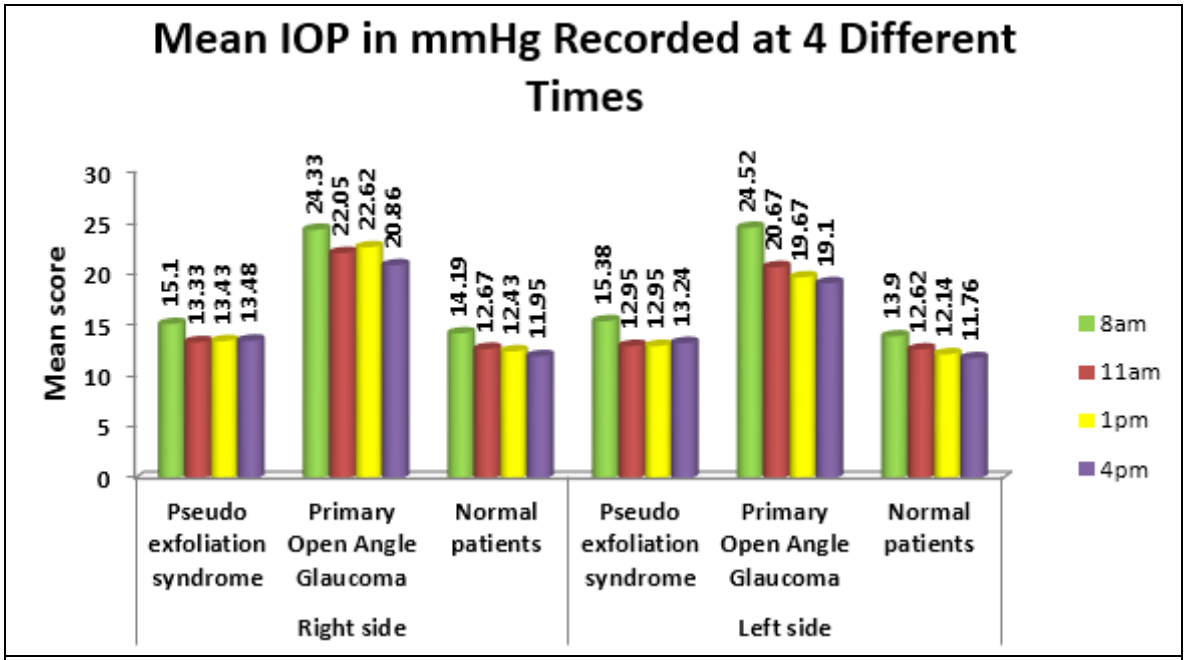

Graph 4: Comparision of IOP among 3 groups in both eyes at 4 different times of the day

DISCUSSION

Pseudoexfoliation syndrome is an ocular manifestation of systemic disorder as it has also been found in skin and visceral organs.[13] It is the commonest cause of secondary open angle glaucoma.Prevalence increases in 6th decade of life. Pseudoexfoliation syndrome may develop into glaucoma by decreasing the aqueous outflow.[14]Pseudoexfoliation glaucoma rapidly progresses than POAG and result in significant visual loss. The pathogenesis is multifactorial but in few populations patients have Single Nucleotide Polymorphisms (SNP) in LOXL1 gene on chromosome.[15]

Central corneal Thickness and Intraocular pressure are greatest in the early morning due to overnight hydration related increase in corneal thickness.

This study aimed at determining the diurnal variation of CCT in patients with Pseudoexfoliation syndrome and comparing with POAG and normal subjects and its effects on IOP. According to Ocular Hypertension Treatment Study, Central Corneal Thickness is regarded as an independent risk factor for glaucoma as it could underestimate or overestimate IOP.[15]

In our study, the PXF group displayed a statistically significant thinner CCT of mean 502.80 µm compared with the POAG and normal individuals and is consistent to previous studies done by Stuart Keel et al.[3,8] It showed a mean variation of 27.49 µm in PXF group compared to normal subjects. The diurnal variation of CCT in PXF group and POAG group during the day is larger than normal individuals.

A statistically significant decrease in CCT in PXF group from 8 a.m. to 4 p.m. may be responsible for the decrease in IOP during the same time period in that group. Thus wide fluctuation in diurnal CCT and IOP is a noteworthy finding, as it is considered to be the major risk factors in the development and progression of glaucoma.

Pseudoexfoliation syndrome showed significant fluctuation in IOP compared to normal individuals with $p \leq 0.05$.[16]This is considered an important risk factor as larger fluctuation in IOP can cause damage to the optic nerve head.[17]

In accordance to the study by Fogagnolo et al in POAG patients, there existed a significant correlation between IOP and CCT.[10] Similarly the results of this study showed that in PXF group a statistically significant correlation does exist between mean CCT and mean IOP.

Strengths of this survey included an age-matched control group.To avoid inter-observer variability, all measurements of IOP and CCT throughout the day was measured by a single examiner

The limitations of our study were small sample size and gender imbalance. Inspite of several studies in this area of research, existence of gender prevalence still remains unclear in PXF syndrome.

CONCLUSION

According to our study, in the study population of PXF without glaucoma, diurnal variation has a significant influence on Central Corneal Thickness. As variation in CCT has a direct confounding effect on underestimating Intraocular pressure, it calls attention to the importance of measuring CCT in this population. Due to wide variation of IOP during the day, close monitoring and frequent follow ups for patients with pseudoexfoliation is needed and resetting and re-evaluation of target IOP must be done with closer emphasis on IOP. Close monitoring of IOP and CCT is emphasized in PXF group without glaucoma for the early detection and prompt treatment

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of glaucomatous damage and prevention of further damage and progression of the disease.

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