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Effect of Primary Pterygium on Corneal Endothelial Cell Density

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Running title: Effect of primary pterygium on corneal endothelial cell density.

Abstract

Purpose: Study effect of unilateral primary pterygium on corneal endothelial cell density.

Patients and Methods: a cross sectional observational comparative study was conducted on 30 patient with unilateral primary pterygium who were attended to Mansoura ophthalmic center on the period from September 2019 to September 2020 to assess corneal endothelial cell density, coefficient of variation, central corneal thickness using a non-contact specular microscopy. The contralateral eye served as a control.

Results: Thirty patients were included in the study, 19 male (63.3%) and 11 female (36.7%). There was statistically significant reduction in the mean corneal endothelial cell density (cells/mm) in eyes with pterygium compared to control eyes (2423.10 ± 248.97 vs 2539 ± 256.39 respectively with p value < 0.001). With no statistically significant difference in coefficient variation and central corneal thickness in pterygium eyes and control eyes.

Conclusion: pterygium eyes were associated with significant reduction in corneal endothelial cell density compared to contralateral control eyes.

Key words: pterygium, corneal endothelium, specular microscopy, corneal thickness, coefficient variation.

INTRODUCTION:

Pterygium is a proliferative growth of fibro vascular tissue that cross the limbus and extend over the cornea.[1] It is characterized by epithelial proliferation, epithelial mesenchymal transition, inflammation and matrix remodeling.[2] It is one of the most common important disorder that influence visual performance of the eye.[3]

Pathophysiology of pterygium remains unclear. But it is thought that ultraviolet ray's exposure is the most important cause for pterygium development, also chronic irritation and inflammation occurring at the ocular surface may have a role in its development.[4, 5]

Ultra violet (UV) rays has been shown to induce Proinflammatory cytokines, chronic inflammatory cells DNA damage.[6] Proinflammatory cytokines activates transforming growth factor beta (TGF-beta) that inhibits MMPs which reduce collagen solubilization.[7]

Pterygium cells that invade the bowman membrane can trigger elevation of matrix metalloproteinase (such as MMP-1, MMP-2, MMP-9) expression, causing dissolution of hemi

desmosome attachments leading to deep corneal changes that involve Descemet membrane and endothelium.[8, 9]

Corneal endothelium is composed of single layer of flat, hexagonal cells which line posterior surface of the cornea and can't regenerate. It maintains the corneal stroma in a continuous dehydration state of through its two main actions barrier and pump functions. Any compromise in these activities will lead to loss of corneal transparency and interfere with vision.[10-13]

It is predicted that primary pterygium may affect corneal endothelial cell density (ECD) so, this study planned to evaluate ECD in cases with unilateral primary pterygium using non-contact specular microscopy and contralateral eye served as a control.

Patients and methods:

This was a Cross sectional observational comparative study. This study was conducted on thirty patients attending to Mansoura Ophthalmic Center on the period from September 2019 till September 2020.It was including patients with unilateral pterygium of any age and both sex and excluding patients with recurrent pterygium, who had past history of ocular surgery or any ocular disease that may affect corneal endothelium like Glaucoma, uveitis, history of Trauma and Contact lens user. A good quality endothelial cell count image was assessed by non-contact specular microscopy. The contralateral eye of each patient was served as a control.

A full ophthalmic examination was done including: Best corrected visual acuity assessment using landolt broken ring charts then converted to LOG MAR. Slit lamp examination of anterior segment (conjunctiva, cornea, anterior chamber, pupil, iris and crystalline lens), Refraction using auto refractometer (Topcon RM-800), Ocular tension measurement using goldmann applanation tonometer, Non-contact Tomey EM-3000 specular microscopy (Tomey corporation, Nagoya, Japan) to measure: Corneal endothelial cell density, Central corneal thickness and Rate of polymegathism represented by coefficient of variation, corneal topographer (Tomey TMS-5, Nagoya Japan) to assess Corneal astigmatism in 3 mm, Central corneal thickness and mean corneal power.

Non-contact specular microscopy:

The patient asked to look straight ahead and keep their eyes open as wide as possible during scanning. When a blue cross appear the image will captured automatically, then analysis of the captured image. Corneal endothelial cell density at central cornea, central corneal thickness and rate of polymegathism which represented by coefficient of variation were measured bilaterally (comparing pterygium eye with control healthy eye) All measurements were done by one person at a single clinical site.

Figure 1: Non-contact Tomey EM-3000 specular microscopy

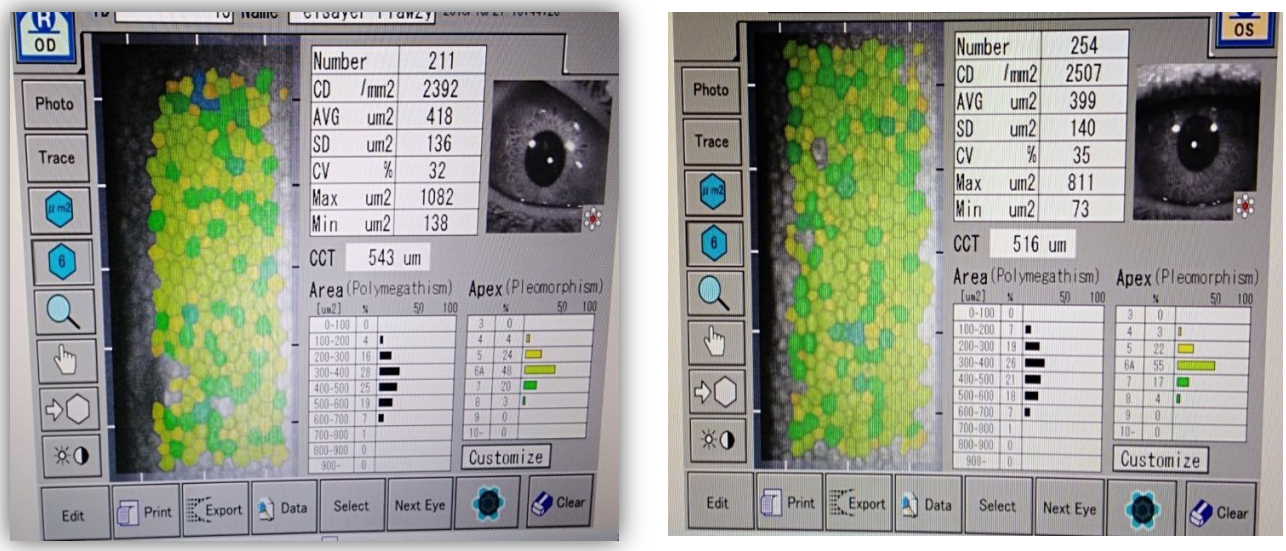

Figure 2: analysis of specular microscopy image in patient with unilateral right pterygium

Pterygium eye (right)		*Control eye (left)*
2392 mm2	Endothelial cell density (CD)	2507 mm2
32%	Coefficient variation (CV)	35 %
543 µm	Central corneal thickness (CCT)	516 µm

Statistical analysis of the data:

IBM's SPSS statistics (Statistical Package for the Social Sciences) for windows (version 25, 2017) was used for statistical analysis of the collected data. All tests were conducted with 95% confidence interval. P (probability) value < 0.05 was considered statistically significant. Charts were generated using SPSS' chart builder and Microsoft Excel for windows 2019.

Ethics approval and consent to participate:

This cross-sectional study was approved by Mansoura Medical Research Ethics Committee, Faculty of Medicine, Mansoura University (code number MS.19.10.858). All subjects provided written informed consent prior to study participation.

RESULTS:

Thirty patients, 19 male (63.3%) and 11 female (36.7%) patients were included in the study. All patients had unilateral primary pterygium that invaded the cornea. The measured parameters were evaluated using IBM SPSS software (Table 1).

Table (1): Compares studied data results between pterygium eyes and controls.

	Pterygium eyes (n = 30)	Control eyes (n = 30)	P value
BCVA mean (SD)	0.29 ± 0.317	0.31 ± 0.481	0.631
ECD mean (SD)	2423.10 ± 248.97	2539.53 ± 256.39	<0.001
CV mean (SD)	0.38 ± 0.047	0.37 ± 0.038	0.160
CCT mean (SD) in SM	509.87 ± 30.036	505.70 ± 26.135	0.102
AST mean (SD)	1.75 ± 1.625	0.52 ± 0.499	<0.001
CCT mean (SD) in topography	515.50 ± 31.582	512.70 ± 26.810	0.633
Corneal power mean (SD)	43.47 ± 1.580	44.01 ± 1.835	0.067
P value is significant when < 0.05			

BCVA=Best corrected visual acuity, ECD = endothelial cell density, CV = coefficient variation, CCT = central corneal thickness, AST = astigmatism in 3 mm, SM = specular microscopy

ECD in pterygium eyes was statistically significantly lower than control eyes (2423.10 ±248.97 vs 2539.53 ± 256.39 p value <0.001) with insignificant increase in CV and CCT of pterygium eyes than controls (0.38 ± 0.047 vs 0.37 ± 0.038 and 509.87 ± 30.036 vs 505.70 ± 26.135) (figure 3-5)

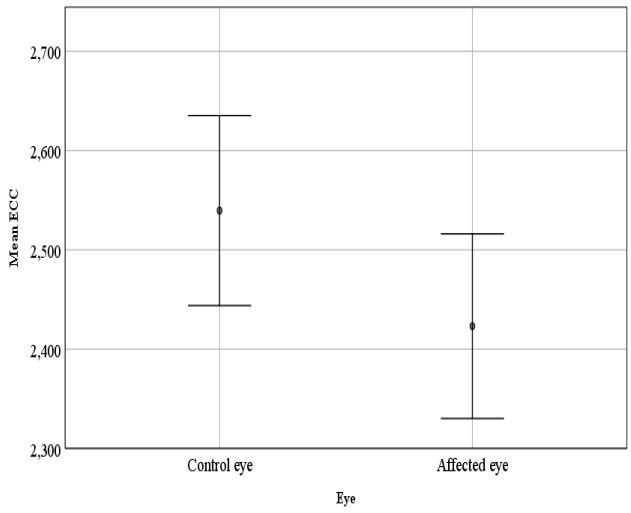

Figure 3: Endothelial cell count in Specular microscopy among studied groups

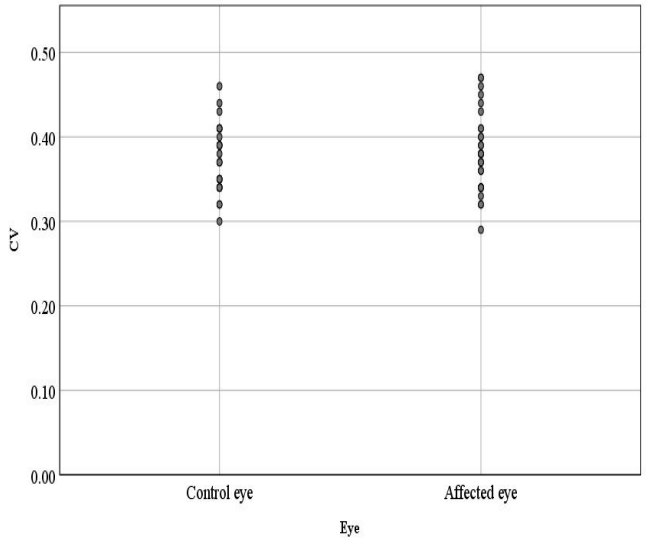

Figure 4: Coefficient variation in Specular microscopy among studied groups

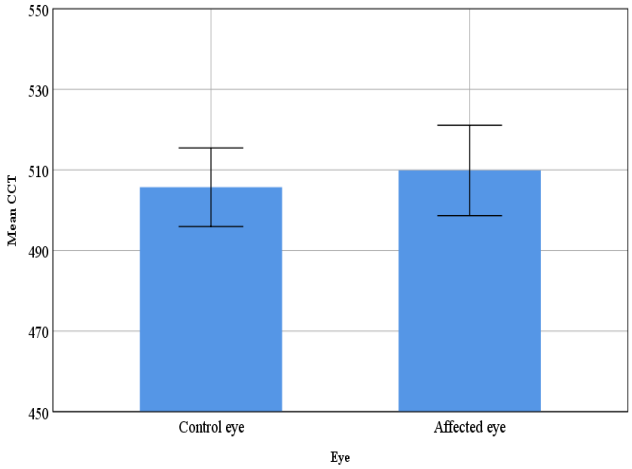

Figure 5: Central corneal thickness in Specular microscopy among studied groups

Correlations were assessed using Pearson correlation coefficient. There was negative correlation between pterygium presence and (BCVA, ECC) and positive correlation between pterygium presence and CCT, and (table 2).

Table 2: Correlation between pterygium presence and studied variables:

	Correlation coefficient	P value
BCVA	-0.035	0.789
ECC	-0.228	0.080
CV	0.110	0.401
CCT Specular microscopy	0.075	0.569

P is significant when < 0.05.

BCVA = Best corrected visual acuity, ECC = Endothelial cell count, CV = coefficient variation, CCT = central corneal thickness.

DISCUSSION:

Pterygium is a common degenerative disease that affect the cornea and may be associated with changes in different corneal layers including corneal endothelium[14,15] which is considered an important factor in maintaining corneal clarity through its pump

and barrier functions and any reduction in ECD will cause loss of clarity and interfere with vision.[16, 17]

Our cross-sectional observational study aimed to evaluate effect of unilateral primary pterygium on ECD. It included thirty patient 19 male (63.3%) and 11 female (36.7%) patients unilateral primary pterygium that invaded the cornea. Non-contact Tomey EM 3000 specular microscopy were used to assess corneal endothelial cell density in both eyes and contralateral eye served as a control.

In our study, ECC in eyes with pterygium was 2423.10 ± 248.97 with significant reduction compared to control eyes which was 2539.53 ± 256.39. (P value < 0.001). CV in eyes with pterygium was 0.38 ± 0.047 with mild insignificant increase than control eyes which was 0.37 ± 0.038, and CCT show insignificant increase in CCT in eyes with primary pterygium compared to control eyes. (509.87 ± 30.036 VS 505.70 ± 26.135). Reduction in ECD may be attributed to Ultraviolet light over exposure as it is considered the most significant risk factor for pterygium development also, ultraviolet light radiation may trigger inflammation, oxidative damage and apoptosis of the ECC, leading to ECC loss.

Several studies were matched with our study, Sousa et al.,[8] study reported that the mean corneal ECD (cells/mm) was lower in the pterygium eyes than in the controls (2451.83 ± 284.96 vs. 2549.95 ± 268.94. Hsu et al.,[14] study included Ninety patients with unilateral primary pterygium The median of ECD in pterygium eyes was lower than controls, it was 2232 cells per square millimeter in eyes with pterygium, and 2463 cells per square millimeter in control eyes. In addition, Li et al.,[4] study reported that UV radiation exposure played a significant role in the effect of pterygium in decreasing the corneal ECD. Ahmed et al.,[18] study show The mean of ECD was lower in eyes with late stage pterygium (2156.2 ± 138.9) than early stage (2496.7 ± 92.1) and control eyes (2498 ± 100.6).

On the other hand Hu et al.,[19] study found out that Primary pterygium may not be associated with a decrease in endothelial cell density in study population of rural Chinese patients (2,485 ± 315 cells/mm2 in pterygium eyes)VS (2,492 ± 312 cells/mm2 in control eyes, p = 0.84), Also, Zhang et al.,[20] study reported that no difference in ECD between pterygium and non-pterygium groups which was 2600 ± 436 vs 2602 ± 421. Insignificant effect of primary pterygium on ECD may be due to in adequate exposure to ultraviolet rays or corneal endothelial cells may adapt to ultraviolet radiation.

Ahmed et al., and Hsu et al.,[14,18] studies reported insignificant increase in the coefficient of variation between eyes with pterygium and control eyes that was matched with our study. While Sousa et al.,[8] study reported insignificant reduction in CV in eyes with pterygium compared to control eye. Li et al., Sousa et al., Mootha et al.,[4,8,15] studies were matched with our study and reported that CCT of pterygium eyes found to be thicker than that of control eye but statistically insignificant. On the other hand these studies[21, 22] reported in significant reduction in CCT in pterygium eyes than that of healthy eyes

Limitations:

Our study had some limitations first we couldn't document long term effect of pterygium on corneal endothelium. Second, we couldn't know frequency of exposure of patients to ultraviolet radiation.

CONCLUSION:

Presence of pterygium affect different corneal layers including corneal endothelium and cause significant reduction in ECD which may have impact on corneal transparency, so it is important to assess corneal endothelial state to maintain corneal clarity. Further studies are recommended for assessment of its effect on corneal microstructures.

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Ethics declarations

Conflict of interest

Doaa S. El Bagalaty, MS, Rania K. Farag, MD, Sherief E. El-Khouly, MD, Mohamed A. Khalaf, all authors have no conflicts of interest that are directly relevant to the content of this review.

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