Journal of Medical and Health Studies
ISSN: 2710-1452
DOI: 10.32996/jmhs
Journal Homepage: www.al-kindipublisher.com/index.php/jmhs

JMHS
AL-KINDI CENTER FOR RESEARCH AND DEVELOPMENT

| RESEARCH ARTICLE

Effect of Primary Pterygium on Endothelial Cell Density

Marwah Mahammed Moftah[1] ✉ and Yasmena Mahmod Abdulhadi[2]
[1] *Department of Ophthalmology, Faculty of Medicine, Benghazi University, Libya*
[2] *Assistant Professor, Ophthalmology Department, Medical College, Benghazi University, Libya*
Corresponding Author: Marwah Mahammed Moftah, **E-mail**: mero121644@gmail.com

| ABSTRACT
Pterygium is a proliferation of fibrovascular tissue over the cornea, causing inflammation and neovascularization. Risk factors include genetic predisposition and chronic environmental irritation. Four grades exist, affecting the corneal limbus, pupil, and pupillary area. Pterygium formation causes flattening of the horizontal meridian and changes in corneal layers to determine if there is a correlation between primary Pterygium and a decrease in corneal endothelial cell density (ECD). This cross-sectional random observational comparative study analyzed 50 patients at Benghazi Teaching Eye Hospital from December 2023 to February 2024. Patients with unilateral pterygium were included. The study assessed endothelial cell count using non-contact specular microscopy and analyzed the corneal endothelial parameters using a Topcon Specular Microscope. The study participants were 74% male, with a mean age of 53.74 +11.06 years. Pterygium grading revealed that 36% had grade one, 62% had grade two, and only 2% had grade three. The study found a significant difference in endothelial cell density between the case and control groups($p<0.001$), with the case group having a lower mean ECD than the control group. Central corneal thickness was also significantly different between eyes with primary pterygium invasion and those without($p<0.001$). However, the Kruskal-Wallis Test showed no significant association between pterygium grading and endothelial cell density($p>0.05$). Primary pterygium significantly affects corneal endothelial cell density and central corneal thickness. Further research is needed to understand its clinical implications and correlation with pterygium progression. Understanding pterygium's impact on corneal health and the regularity of astigmatism could improve management and treatment options.

| KEYWORDS

Pterygium; Endothelial Cell Density; inflammation; neovascularization

| ARTICLE INFORMATION

ACCEPTED: 01 June 2024 **PUBLISHED:** 08 June 2024 **DOI:** 10.32996/jmhs.2024.5.2.14

1. Introduction
Pterygium is a proliferation of fibrovascular tissue of bulbar conjunctiva that extends over the cornea and crosses the limbus[Nejima, 2015]

There are various known risk factors as genetic predisposition and chronic environmental irritation—which include UV (ultraviolet) rays, hot, dry weather, wind, dusty atmosphere, and the period of exposure to such conditions; however, the most common is the increased time of exposure to UV rays of the sunlight dry and dusty, followed by chronic eye irritation that leading to increasing pro-inflammatory cytokines, lead to the conjunctival matrix remodeling from conditions [Li, 2018][Bradley, 2010]conversion of inactive fibroblasts into activated ones thereby causing local inflammation and neovascularization[Cardenas-Cantu, 2016]. Recent research has suggested that the pathophysiology of the pterygium may also involve the human papillomavirus [Reid, 2003]

As a result, four grades can be defined: grade I invades the corneal limbus; grade II approaches the pupillary area and surpasses the limbus; grade III reaches the pupil; and grade IV exceeds the pupil·[Tan, 1997]

Previous studies have shown that the development of pterygium causes the horizontal meridian along its leading head to flatten, which usually results in with-the-rule astigmatism[Tomidokoro, 2000] and corneal astigmatism according to anterior corneal curvature measurements [McCarey, 2008]

Certain proteases produced by the pterygium head facilitate invasion. Research has indicated that the pathological and biochemi cal alterations brought about by pterygium formation also serve as a precursor to changes in the deep layers of the cornea[Yang, 2009]

When pterygium cells dissolve through the Bowman membrane, they can increase the expression of matrix metalloproteinases (like MMP-1, MMP-2, and MMP-9), which can lead to the breakdown of hemi desmosome attachments and deep alterations in the cornea that affect the endothelium and Descemet membrane. [Yang, 2009; Sousa, 2017]

2. Aim of study

The main goal of this study is to correlate if there is a relationship between primary Pterygium and a decrease in the corneal endothelial cell density (ECD)

2.1 Patients and Methods

Study design This was a cross-sectional random observational comparative study.

Study setting This study was conducted on fifty patients attending Benghazi Teaching Eye Hospital from December 2023 to February 2024.

Inclusion criteria It included patients with unilateral pterygium of any age or gender.

Exclusion criteria patients with recurrent pterygium, who had a history of ocular surgery or any ocular disease that may affect corneal endothelium like Glaucoma, uveitis, History of Trauma, and Contact lens use.

A good quality endothelial cell count image was assessed by non-contact specular microscopy. The contralateral eye of each patient served as a control. A full ophthalmic examination was done, including the best corrected visual acuity assessment using landolt broken ring charts, which were then converted to LOG MAR. Slit lamp examination of the anterior segment (conjunctiva, cornea, anterior chamber, pupil, iris, and crystalline lens), Refraction using an auto refractometer, Ocular tension measurement using Goldmann applanation tonometer, Endothelial cell density will measure by Specular microscopy Corneal endothelial parameters and Quantitative analysis of cell count will be recorded using Topcon Specular Microscope (SP-1P model) including:

- Central corneal thickness (CCT) in µm
- Endothelial cell density (ECD) in cells/mm2
- Percentage of Hexagonal cells (HEX)
- Coefficient of variation (CV)

2.2 Non-contact specular microscopy

During the scanning process, the patient is instructed to look straight ahead and to keep their eyes as wide open as possible. An automatic image capture occurs when a blue cross appears. The captured image is then analyzed. Measurements of corneal endothelial cell density at the central cornea and corneal thickness at the center, as indicated by the coefficient of variation, were taken bilaterally (comparing the pterygium eye with the healthy control eye). One individual performed all of the measurements at a single clinical site (figure 1).

Figure 1. Non-contact Topcon Specular Microscope (SP-1P model)

Statistical analysis The statistical analysis was performed using IBM's SPSS statistics software (Statistical Package for the Social Sciences) for Windows, version 25. A P-value less than 0.05 was set as statistically significant. The charts were created using Microsoft Excel for Windows 2019.

3. Results

The study population consisted of 50 participants (100 Eye), with the majority being male (74%) and the mean age of the group being 53.74 $\pm$11.06 years with a range from 30 to 80 years. Pterygium grading revealed that 36% had grade one, 62% had grade two, and only 2% had grade three. These baseline characteristics provide important demographic information for understanding the results of the study on central corneal thickness in eyes with primary pterygium invasion (Table 1).

The study found that there was a significant difference in endothelial cell density between the case group and the control group, with the case group having a lower mean ECD of 2561.9 cells/mm2 compared to the control group's mean ECD of 2656.3 cells/mm2 ($p < 0.001$). The results of the study revealed a statistically significant difference in central corneal thickness between eyes with primary pterygium invasion and those without ($p < 0.001$), as the mean values were 506.7 µm for case and 516.5µm for controls (Table 2).

The results of the Kruskal-Wallis Test showed no significant association between pterygium grading and endothelial cell density (P=0.841). (Table 3)

Table 1. Baseline characteristics of the study population

Character	N	%
Gender		
Male	37	(74%)
Female	13	(26%)
Mean age	53.74	$\pm$(11.063)
Pterygium grading		
Grade one	18	(36%)
Grade two	31	(62%)
Garde three	1	(2%)

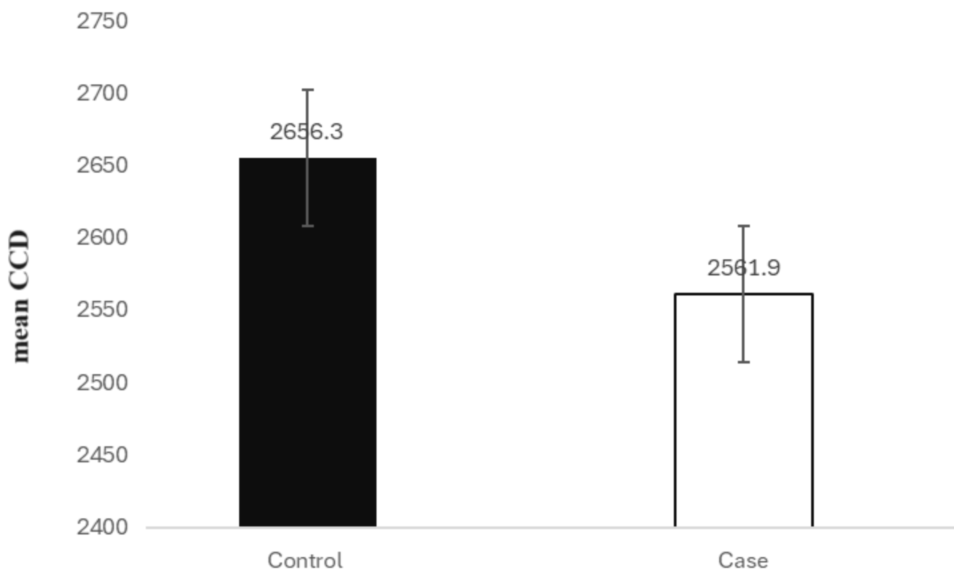

Figure 1. Corneal cell density in Specular microscopy among studied groups

Table 2 Comparison of the studied data results between pterygium eyes and controls

Parameter	Case N=50	Control N=50	P value
ECD mean (SD)	2561.9 (259.8)	2656.3 (277.8)	**<0.001***
CCT mean (SD) in SM	506.7 (31.3)	516.5 (24.9)	**<0.001***
CV mean (SD)	0.33 (0.036)	0.33 (0.04)	0.962
HEX mean (SD)	0.52 (0.072)	1.6 (7.6)	0.333

ECD = endothelial cell density, CV = coefficient variation, CCT = central corneal thickness,

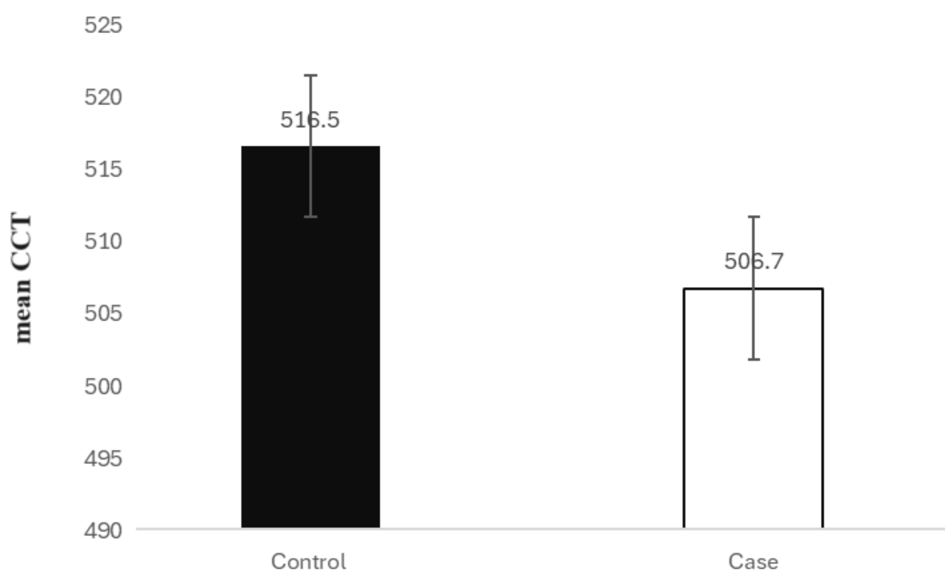

Figure 2. Central corneal thickness in Specular microscopy among studied groups

Table 3. Association between pterygium grading and endothelial cell density (Kruskal-Wallis Test)

Grading	Rank	P value
Grade 1	25.72	0.841
Grade 2	25.65	
Grade 3	17	

4. Discussion

This paper supports the notion that primary pterygium invasion of the cornea may hurt endothelial cell density. Future research should delve deeper into the potential long-term consequences of decreased endothelial cell density in patients with pterygium; this finding matches with many previous studies [Sousa, 2017; Doaa, 2021; Zaidi, 2021; Al-Rubaye, 2021] the endothelial cell density (ECD) of the cornea was associated with a significant reduction in corneal endothelial cell density compared to contralateral; also studies show that corneal ECD (cells/mm) is lower in pterygium eyes compared to controls.

The result of this study shows no significant difference in ECD related to the pterygium grading; in contrast, Studies show that late-stage pterygium eyes have lower mean ECD than early and control eyes[Sousa, 2017; Zaidi,2021; Al-Rubaye, 2021]

Pterygia, a condition characterized by an invasive front of the pterygium epithelium transitioning into corneal epithelium, is not entirely understood [Chui, 2011]. Common histological features include inflammatory cells, cytokines, and enzymes in pterygium cells[Chui, 2011], [Kria, 1996]. These chronic inflammatory components and angiogenesis may work together to degrade BL, a characteristic feature of pterygia. Pterygium invasion may induce deeper changes in the cornea at the endothelium and Descemet membrane, resulting in lower corneal ECD in eyes with pterygium than in the control group [Mootha, 2004]. The presence of pterygia is associated with deep corneal changes at the endothelium and Descemet membrane, with a decrease in corneal ECD in eyes with pterygium involvement. Different corneal measurements, such as corneal thickness and steeper corneas, could impact ECD analysis [Müller, 2004].

This suggests that the presence of pterygium may contribute to a decrease in the thickness central cornea. In line, these studies found a significant decrease in CCT in eyes with pterygium compared to healthy eyes.[Li, 2018], [Sousa, 2017], [Mootha, 2004] Conversely, studies observed that the central corneal thickness (CCT) of eyes with pterygium was thicker than that of control eyes, although the difference was not statistically significant [Ali, 2017], [K\il\iç, 2015]

The study conducted by Ahmed et al. (2020) and Hu et al. (2014) found that there was no significant decrease in corneal vision (CV) in eyes with pterygium compared to control eyes. Li et al., Sousa et al., which aligns with the findings of our study. Zaidi [2021] conducted studies that found a negligible increase in the coefficient of variation between eyes with pterygium and control eyes.

These results highlight the potential impact of pterygium on corneal health and the need for early detection and intervention. The significant correlation between pterygium size and endothelial cell density underscores the importance of monitoring these patients closely. Future studies should focus on elucidating the mechanisms underlying this relationship and developing targeted treatment strategies to preserve endothelial cell function in patients with primary pterygium.

The results of the statistical analysis revealed no significant difference in the HEX mean between the pterygium eye and the healthy control eye. This indicates that there is no measurable variation in corneal endothelial cell density between the two groups. The same results were conducted by Hu et al.; a prospective study showed no significant difference in hexagonal between pterygium and contralateral eyes.[Hu, 2020]. In Contrast, the Hexagonal cell was found to be statistically significantly different between pterygium and contralateral eyes [Al-Rubaye, 2021].

The limitation of the current study was that the study sample was limited in size as a result of the brief timeframe allocated for patient consultations. In addition, certain patients abstained from subsequent visits and examinations, as they were restricted to only the initial examination. However, it is important to note that certain situations may necessitate ongoing medical follow-up to prevent the condition from recurring.

5. Conclusion

Overall, the findings suggest that primary pterygium has a significant impact on corneal endothelial cell density and central corneal thickness. However, further research with a larger sample and covering a broader geographic area is needed to fully understand the implications of these findings and their potential clinical significance.

6. Recommendation

Further studies should focus on investigating the potential correlation between changes in corneal parameters and the progression of pterygium. Additionally, it would be beneficial to explore the impact of pterygium on other aspects of corneal health, such as corneal regularity of astigmatism. Understanding these factors could lead to improved management and treatment options for patients with pterygium**.**

Acknowledgment We express our gratitude to Sara Momamed. A. M. Bogazia, an Assistant lecturer in the Department of Oral Biology at the Faculty of Dentistry, Ajdabiya University, for conducting the statistical analysis and providing a valuable language review of this publication.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

Publisher's Note: All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers.

References

[1] Ali R. T. E. and Ali A. B. M., (2017) The effect of pterygium on corneal thickness, corneal curvature, tear volume, and intraocular pressure in a Sudanese Population, *Al-Basar Int. J. Ophthalmol.*, 4, 4, 109–113, 2017.

[2] Ahmed E. S., El Shayeb A. A., and Uosry R. M., (2020) Evaluation of Effect of Pterygium on the Endothieleal Cell Density of the Cornea by Specular Microscopy, *Benha J. Appl. Sci.*, 5, 4 part (2), 211–217, 2020.

[3] Al-Rubaye S. and Al Ajeeli A., (2021) The Effects of Primary Pterygium on Corneal Endothelial Cells Density in Iraqi Eyes, 2, 0–13, Jan. 2021.

[4] Bradley J. C., Yang W., Bradley R. H., Reid T. W., and Schwab I. R., (2010) The science of pterygia, *Br. J. Ophthalmol.*, 94, 7, 815–820, 2010.

[5] Cardenas-Cantu E., Zavala J., Valenzuela J., and Valdez-Garc\'\ia J. E. (2016) Molecular basis of pterygium development, in *Seminars in ophthalmology*, 2016, 31, 6, 567–583.

[6] Chui J., Coroneo M. T., Tat L. T., Crouch R., Wakefield D., and Di Girolamo N., (2011) Ophthalmic pterygium: a stem cell disorder with premalignant features, *Am. J. Pathol.*, 178, 2, 817–827, 2011.

[7] Doaa P., El Bagalaty S., Rania MS K. Farag, MD, Sherief E. El-Khouly, MD and Mohamed A.K, (2021) Effect of Primary Pterygium on Corneal Endothelial Cell Density, *Egypt. J. Ophthalmol.*, 4, 223-230., 2021.

[8] Hsu M.-Y. *et al.*, (2014) Pterygium is related to a decrease in corneal endothelial cell density, *Cornea*, 33, 7, 712–715, 2014.

[9] Hu Y, Atik A, Qi W, and Yuan L. (2020) The association between primary pterygium and corneal endothelial cell density, *Clin. Exp. Optom.*, 103, Feb. 2020, doi: 10.1111/cxo.13049.

[10] Kria L., Ohira A., and Amemiya T., (1996) Immunohistochemical localization of basic fibroblast growth factor, platelet-derived growth factor, transforming growth factor-$β$ and tumor necrosis factor-$α$

[11] K\il\iç R., Çomça S., A\ugaday\i A., and POLAT O., (2015) The effect of pterygium existence on central corneal thickness Pterjiumun santral kornea kalinli{\u{g}}i üzerine etkisinin de{\u{g}}erlendirilmesi, *Duzce Med. J.*, 17, 1, 2015.

[12] Li X., Dai Y., Xu W., and Xu J., (2018) Essential role of ultraviolet radiation in the decrease of corneal endothelial cell density caused by pterygium, *Eye*, 32, 12, 1886–1892, 2018.

[13] Mootha V. V., Pingree M., and Jaramillo J., (2004) Pterygia with deep corneal changes, *Cornea*, 23, 6, 635–638, 2004.

[14] Müller A., Craig J. P., Grupcheva C. N., and McGhee C. N. J., (2004) The effects of corneal parameters on the assessment of endothelial cell density in the elderly eye, *Br. J. Ophthalmol.*, 88, 3, 325–330, 2004.

[15] McCarey B. E., Edelhauser H. F., and Lynn M. J., (2008) Review of corneal endothelial specular microscopy for FDA clinical trials of refractive procedures, surgical devices, and new intraocular drugs and solutions, *Cornea*, 27, 1, 1–16, 2008.

[16] Nejima R., Masuda A., Minami K., Mori Y., Hasegawa Y., and Miyata K. (2015) Topographic changes after excision surgery of primary pterygia and the effect of pterygium size on topographic restoration. *Eye Contact Lens*, 41, 1, 58–63, Jan. 2015, doi: 10.1097/ICL.0000000000000065.

[17] Reid T. W. and Dushku N., (2003) Does human papillomavirus cause pterygium?, *British Journal of ophthalmology*, 87, 7. BMJ Publishing Group Ltd, pp. 806–808, 2003.

[18] Sousa H. C. C., Silva L. N. P., and Tzelikis P. F., (2017) Corneal endothelial cell density and pterygium: a cross-sectional study, *Arq. Bras. Oftalmol.*, 80, 317–320, 2017.

[19] Tan D. T. H., Chee S.-P., Dear K. B. G., and Lim A. S. M., (1997) Effect of pterygium morphology on pterygium recurrence in a controlled trial comparing conjunctival autografting with bare sclera excision, *Arch. Ophthalmol.*, 115, 10, 1235–1240, 1997.

[20] Tomidokoro A., Miyata K., Sakaguchi Y., Samejima T., Tokunaga T., and Oshika T., (200) Effects of pterygium on corneal spherical power and astigmatism, *Ophthalmology*, 107, 8, 1568–1571, 2000.

[21] Yang S.-F., Lin C.-Y., Yang P.-Y., Chao S.-C., Ye Y.-Z., and Hu D.-N., (2009) Increased expression of gelatinase (MMP-2 and MMP-9) in pterygia and pterygium fibroblasts with disease progression and activation of protein kinase C, *Investig. Ophthalmol. \& Vis. Sci.*, 50, 10, 4588–4596, 2009.

[22] Zaidi S. B. H. and Ali K W., (2021) Is Pterygium Morphology Related to Loss of Corneal Endothelial Cells? A Cross-Sectional Study., *Clin. Ophthalmol.*, 15, 1259–1266, 2021, doi: 10.2147/OPTH.S296531.