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Corneal Endothelial Cell Density and Morphology in Healthy Libyan Eyes

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Abstract

Background Endothelial cell density and morphology vary across ethnic groups.
Aim This article investigates the corneal endothelial cell density and morphology in healthy Libyan eyes.
Methods A 3-month cross-sectional observational study was conducted at Benghazi Teaching Eye Hospital, involving 198 eyes of 100 healthy Libyan participants. The noncontact Topcon specular microscope (SP-1P model) was used to assess the following parameters: the mean central corneal thickness (CCT), the mean cell density (MCD), the mean coefficient of variation (CV%), and the mean percentage of the hexagonal cell (Hex [%]). The variables were analyzed in relation to age and gender using the Statistical Package for the Social Sciences (SPSS version 25.0)
Results The mean age of participants in this study was 47.4 ± 13.8 years (range 21–75 years). The mean CCT was 516.45 ± 43.04 μm, the MCD was 2664.30 ± 371.26 cells/mm^2, the mean CV% was 32.3% ± 3.7, and the mean Hex (%) was 52.8% ± 9.6. There was no statistical difference in the age, CCT, and MCD across genders. Whereas CV (%) and Hex (%) showed significant gender differences ($p < 0.01$ for both). There was a significant negative weak correlation between CCT ($r = -0.10$) and age, as well as a significant negative moderate correlation between MCD and Hex (%) with age ($r = -0.36$ and $r = -0.31$, respectively). CV% exhibited a significant, moderately positive association with age ($r = 0.35$). The higher endothelial cell loss rate of 8.4% was in the third decade of life whereas other age groups ranged between 1.1 and 2.7%.
Conclusion The normative data for the endothelium of Libyan eyes are reported, which can be used as a baseline for future studies.

Keywords
► corneal endothelium
► Libyan eyes
► morphology
► normative data
► specular microscopy

* *The study was carried out following the Helsinki Declaration, and the subjects signed an informed consent form after being informed about the study.*

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ملخص المقال باللغة العربية

كثافة الخلايا البطانية للقرنية وتشكلها في العيون الليبية السليمة

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خلفية: تختلف كثافة الخلايا البطانية وتشكلها بين المجموعات العرقية..

الهدف: دراسة كثافة الخلايا البطانية القرنية وتشكلها في العيون الليبية السليمة.

الطُرق: أجريت دراسة رصدية مقطعية لمدة ثلاثة أشهر في مستشفى العيون التعليمي ببنغازي، شملت 198 عيناً من 100 مشارك ليبي سليم. تم استخدام مجهر Topcon براق نموذج SP-1P لتقييم المعلومات التالية؛ متوسط سمك القرنية المركزي (CCT)، ومتوسط كثافة الخلية (MCD)، ومتوسط معامل التباين (CV%)، وكذلك النسبة المئوية المتوسطة للخلية السداسية (٪). تم تحليل المتغيرات بالنسبة للعمر والجنس باستخدام الحزمة الإحصائية للعلوم الاجتماعية (SPSS).

النتائج: كان متوسط عمر المشاركين في هذه الدراسة 47.4 ± 13.8 سنة (يتراوح بين 21 و75 سنة)، 60% من الحالات كانت ذكوراً. كان متوسط سمك القرنية المركزية 43±516.45 مايكرومتر، وكان متوسط كثافة الخلايا 2664±371 خلية/مم2، وكان متوسط معامل التباين 32.3±3.7%، ومتوسط النسبة المئوية للقرنية السداسية كانت 52.8%±9.6 خلية. لم يكن هناك فرق إحصائي في العمر، ومتوسط سمك القرنية المركزي، ومتوسط كثافة الخلايا بين الجنسين، في حين أن متوسط معامل التباين (٪) ومتوسط النسبة المئوية للخلية السداسية (٪) أظهرا اختلافات ذا دلالة إحصائية بين الجنسين. كان هناك ارتباط سلبي ضعيف معنوي بين متوسط سمك القرنية المركزي والعمر (r= -0.10)، بالإضافة إلى وجود ارتباط سلبي معتدل معنوي بين متوسط كثافة الخلية (r= -0.36) ومتوسط النسبة المئوية للخلية السداسية (r= -0.31) مع العمر. أظهر متوسط معامل التباين ارتباطًا إيجابيا كبيرا إلى حد ما مع العمر (r = 0.35).
كان معدل فقدان الخلايا البطانية الأعلى بنسبة 8.4٪ في العقد الثالث من العمر بينما تراوح الفقدان للفئات العمرية الأخرى ما بين 1.1% و2.7%.

الاستنتاج: هذه دراسة عن البيانات المعيارية لبطانة العيون الليبية، والتي يمكن استخدامها كأساس للدراسات المستقبلية.

الكلمات المفتاحية: بطانة القرنية، العيون الليبية، التشكل، البيانات المعيارية، المجهر المرآوي.

Introduction

The corneal endothelium is a single layer of hexagonal cells covering the inner surface of the cornea. It acts as a barrier between the corneal stroma and the aqueous humor, limiting the passage of water and solutes from the anterior chamber to the interior of the stroma. The endothelial cells have a crucial transport protein, the metabolic-endothelial pump of electrolytes, which is $Na+/K+$/ATPase-dependent. This pump counteracts the flow of water into the cornea, which is vital in maintaining the normal state of relative dehydration of the corneal stroma essential for corneal transparency.[1]

Endothelial cells do not reproduce. In adults, the density varies between 2,000 to 3,000 cells/mm^2 and declines with age. The minimum level of cells necessary for normal function is estimated to be between 600 and 900 cells/mm^2, from this limit stromal edema appears.[2] The endothelium is metabolically very active and is primarily responsible for corneal transparency. The cornea maintains a constant thickness throughout life and retains its aqueous content at a stable level of relative dehydration. The anatomical integrity of the corneal endothelium is one of the most important factors that directly influence the cornea's hydration rate.[3]

Specular microscopy is a diagnostic technique that allows us to obtain images with high magnification of endothelial cells. It provides a clear view of living cells, without altering their function or morphology. Using this test, an endothelial count by surface area can be performed to determine any alteration in the shape or size of endothelial cells. These parameters give us a framework for assessing the functional capacity of the endothelium. Specular microscopy is a diagnostic test of great clinical utility, especially for cases that require a second intraocular intervention, such as operated cases or when a primary endothelial alteration is suspected.[4]

Due to the significant variation in endothelial density found in different ethnic groups and by age, it is essential to know the normal data in each population.[3]

Thus, this study aimed to investigate the corneal endothelial cell density and morphology in healthy Libyan eyes at Benghazi Teaching Eye Hospital.

Methods

A cross-sectional, observational study was conducted at Benghazi Teaching Eye Hospital, Benghazi, Libya, from December 2023 to April 2024, which included 198 eyes of 100 healthy white Libyan individuals (two eyes were excluded; one with corneal scar and the other one with a pterygium), randomly selected among the hospital's staff, relatives of patients attending the hospital, and the outpatient department, and anyone who met the inclusion criteria was examined to exclude any ocular pathology to determine their eligibility for the study.

Inclusion Criteria

Subjects free of ophthalmological diseases aged 17 years or more with no history of eye surgery and not a known diabetic or hypertensive.

Exclusion Criteria

Subjects with a refractive error greater than ± 3 diopters, Diabetics, a history of intraocular surgery, ocular trauma, or a history of any intraocular or systemic pathology (like hyperlipidemia, minor ischemic stroke, and gout), contact lens wearer, and those who did not collaborate in performing the examination were excluded.

Table 1 Demographic characteristics and variables related to the corneal endothelial cell characteristics in healthy Libyan subjects

Variable		Number (%)
Gender	Male	60 (60)
	Female	40 (40.0)
Eye	Right eye	100 (50.5)
	Left eye	98 (49.5)
Age	20–30 y	46 (23.2)
	31–40 y	56 (28.3)
	41–50 y	48 (24.2)
	51–60 y	35 (17.6)
	61-70 y	13 (6.7)
	Mean ± SD	47.8 ± 13.8
	Median (range)	51 (21–75)
CCT (µm)	Mean ± SD	516.45 ± 43.04
	Median (range)	513 (465–642)
MCD (cells/mm^2)	Mean ± SD	2664.30 ± 371.26
	Median (range)	2622 (1093–3877)
CV (%)	Mean ± SD	32.3 ± 3.7
	Median (range)	31.2 (16–48)
Hex (%)	Mean ± SD	52.8% ± 9.6
	Median (range)	55 (20–75)

Abbreviations: CCT, central corneal thickness; CV, coefficient of variation; Hex, hexagonality; MCD, mean cell density; SD, standard deviation.

All participants underwent a full ophthalmological examination, including a measurement of visual acuity, an intraocular pressure checkup, and a dilated fundus examination to rule out any pathology.

The study was carried out following the Helsinki Declaration, and the subjects signed an informed consent form after being informed about the study.

Specular microscopy was done by the same examiner using the noncontact Topcon specular microscope (SP-1P model).[5] The machine conducted an automatic study of the cornea, it recorded parameters such as central corneal thickness (CCT), mean cell density (MCD), coefficient of variation (CV%) in the cell area, and hexagonality (Hex [%]).

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS version 25.0; IBM Corporation, Armonk, New York, United States) was used. Data were presented as mean ± standard deviation and frequencies.

The Mann–Whitney test was used instead of the Student's *t*-test for nonparametric data, the test was run to determine if there were differences in variables between genders. Visual inspection revealed that the distributions of engagement scores for males and females were similar. Pearson's chi-square analysis was used to compare percentages. Spearman's correlation analysis was used to compare two qualitative variables. The value of *r* is explained as follows: 0.1 to 0.3, weak correlation; 0.3 to 0.5, moderate correlation; and 0.7 to 1, strong correlation. A *p*-value of < 0.05 was considered statistically significant. A linear regression was performed to determine the effect of age on MCD and corneal endothelial parameters.

Results

The mean age of participants in this study was 47.4 ± 13.8 years (range 21–75 years), with a male predominance of 60 men (60%), and the number of right eyes was 100 (50.5%). The mean CCT was 516.45 ± 43.04 µm, the MCD was 2664.30 ± 371.26 cells/mm^2, the mean CV% was 32.3% ± 3.7, and the mean percentage of the hexagonal cell was 52.8% ± 9.6 (►**Table 1**).

There was no statistical difference ($p > 0.05$), in the age, CCT, and MCD between males and females. Whereas CV% and Hex (%) showed significant gender differences ($p < 0.01$ for both) (►**Table 2**).

There was a significant negative weak correlation between CCT ($r = –0.10$) and age, as well as a significant negative moderate correlation between MCD ($r = –0.36$) and Hex ($r = –0.31$) with age. CV exhibited a significant moderate positive association with age ($r = 0.35$) (►**Table 3**).

The higher endothelial cell loss rate of 8.4% was in the age group 31 to 40 years, and ranged between 1.1 and 2.7% in other groups (►**Table 4**).

Discussion

The endothelial cells of the cornea lack regeneration capacity. Thus, a loss in corneal endothelial cell density is compensated for through cell spreading, resulting in increased cellular pleomorphism and a drop in the percentage of hexagonal cells.[6] Many studies have demonstrated that the

Table 2 Comparison of age and endothelial cell characteristics between genders in healthy eyes of Libyan participants

Variables	Men (mean ± SD)	Women (mean ± SD)	*p*-Value[a]
Age	47.6 ± 15.7	47.25 ± 15.3	< 0.754
CCT (µm)	515.2 ± 36.4	511 ± 39.8	< 0.198
MCD (cells/mm^2)	2665 ± 34.2	2635 ± 39.4	< 0.125
CV in cell area (%)	32.7 ± 5.7	31.1 ± 4.8	< 0.012
Hex (%)	53.3 ± 12.1	54.1 ± 11.5	< 0.015

Abbreviations: CCT, central corneal thickness; CV, coefficient of variation; Hex, hexagonality; MCD, mean cell density; SD, standard deviation.
[a]Difference between gender using the Mann–Whitney *U* test.

Table 3 Correlation between age and corneal variables in healthy eyes of Libyan participants

Variables	Spearman's correlation coefficient (*r*)	*p*-Value
CCT (μm)	− 0.109	< 0.009
MCD (cells/mm^2)	−0.365	< 0.001
CV in cell area (%)	0.351	< 0.001
Hex (%)	−0.312	< 0.001

Abbreviations: CCT, central corneal thickness; CV, coefficient of variation; Hex, hexagonality; MCD, mean cell density.

Table 4 Corneal endothelial cell loss in different age groups of Libyan subjects with healthy eyes

Age group (y)	Mean cell density (MCD)	Loss %
20–30	2929 ± 312.6	
31–40	2683 ± 275.2	8.4
41–50	2654 ± 320.14	1.1
51–60	2580 ± 311.3	2.7
60–70	2549 ± 412.3	1.2

density of corneal endothelial cells varies by ethnic origin, age,[6–8] and the model of the instrument.[9]

The causes of endothelial cell insufficiency over time are unknown; however, evidence suggests that apoptosis and/or necrosis caused by light-induced oxidative damage may play a role. In addition, the number of endothelial cells declines following stressful events such as trauma, previous corneal transplantation, stress caused by certain systemic disorders such as diabetes, glaucoma treatment, cataract surgery, and intraocular lens implantation.[10] Therefore, the measurement of endothelial cell density and shape is highly significant, because the decrease in endothelial cell density is a primary indicator of pathological alteration and reduces the ability of corneal healing.[11]

This observational cross-sectional study was conducted in Benghazi Teaching Eye Hospital, over 3 months on 198 eyes of 100 healthy Libyan participants, to investigate the corneal endothelial cell density and morphology in healthy Libyan eyes using the noncontact Topcon specular microscope (SP-1P model).

The mean age of participants in this study was 47.4 ± 13.8 years (range 21–75 years), with 60 males constituting 60% of the cases.

Central Corneal Thickness

In the present study, the mean CCT was 516.45 ± 43.04 μm, which is comparable to the results of the Egyptian[6] (514.45 μm) and Caucasian[9] populations (513 μm), but lower than the Turkish[12] (521 μm) and Indian[7] (533.3 μm) studies (►**Table 5**). These could be attributed to differences in measuring tools, as the Egyptian study used the same noncontact specular microscope as ours, while the other two used different types of specular microscopes. However, a previous study found that people of North African origin had statistically significantly thinner corneas than those of other origins.[13]

There was no statistical difference in the CCT ($p > 0.05$) between males and females, similar to what was previously reported by other studies.[6,12–14]

A statistically significant negative weak correlation between CCT (−0.10) and age was found, which is similar to other studies.[6,15]

The Mean Cell Density

The MCD was 2664.30 ± 371.26 cells/mm^2 which is comparable to the Egyptian[6] (2647.50 cells/mm^2) and Turkish[12] populations (2671 cells/mm^2), higher than Nigerian[16] (2610.26 cells/mm^2) and Iranian[17] populations (1961 cells/mm^2), and lower than Chinese[8] (2932 cells/mm^2) and Caucasian population (2732 cells/mm^2) (►**Table 5**).

Researchers hypothesized an inversely proportionate link between corneal diameter and endothelial cell density to explain the variations in MCD across populations.[7,18] However, we did not measure the corneal diameter in the current study, and no previously published article on the normal corneal diameter of Libyans was found.

There was no statistical difference in the MCD ($p > 0.05$) between males and females in our study, which is consistent

Table 5 Corneal endothelial cell characteristics reported in previous studies compared to the present study

Variables	Age (y) (mean ± SD)	CCT (μm) (mean ± SD)	MCD (cells/mm^2) (mean ± SD)	CV (%) (mean ± SD)	Hex (%) (mean ± SD)
Egyptian[6]	49.48 ± 15.27	514.45 ± 43	2647.50 ± 382	32.31 ± 5.08	53.79 ± 11.00
Indian[7]	48 ± 16.5	533.3 ± 49.7	2525 ± 337	35.8 ± 6.9	57.3 ± 7.9
Caucasian[9]	42 ± 17.1	513 ± 39	2732 ± 305	34 ± 7	46 ± 8
Turkish[12]	44.3 ± 13.5	521 ± 33	2671 ± 356	34.3 ± 5.3	54.9 ± 10.0
Nigerian[16]	50.35 ± 20.13	NR	2610.26 ± 371	43.95 ± 9.50	46.52 ± 8.83
Iranian[17]	52.7 ± 19.1	NR	1961 ± 457	24.1 ± 7.1	NR
Chinese[8]	44 ± 21	NR	2932 ± 363	33 ± 50	59 ± 9
Present study	47.4 ± 13.8	516.45 ± 43.04	2664.30 ± 371.26	32.3% ± 3.7	52.8% ± 9.6

Abbreviations: CCT, central corneal thickness; CV, coefficient of variation; Hex, hexagonality; MCD, mean cell density; NR, not reported; SD, Standard deviation.

with previous studies.[6,12,15,17] However, Padilla et al[19] found that Filipino females had a statistically significantly higher MCD than males ($p < 0.01$), while Yunliang et al[8] found that Chinese males at the age of 61 to 70 years had a statistically significantly higher MCD than females ($p < 0.05$).

An inverse relationship between MCD and age ($r = -0.36$) was found, with the highest rate (8.1%) recorded in the third decade of life which is consistent with previous research.[6,8,12,17] Some researchers explained this by redistributing endothelial cells in the growing cornea,[7,18] while others attributed it to increasing physical activity in this age group.[6]

Researchers reported that the type and model of the specular microscopy instrument can impact the measurements of corneal endothelial cell density.[9,20,21]

The cell loss rate in our study (range 1.1–8.4%) was much higher than in prior studies. In Egypt,[6] the rate of cell loss was 0.1 to 0.7%, in Turkey[12] 1.9 to 5.9%, in Iran[17] 0.6% per year, in China[8] 0.3% per year, and in Japan[22] 0.42%/year, although the exact cause of this higher cell loss in Libyan population is not known; this could be due to ethnic variations.

Coefficient of Variation

This is the most sensitive biomarker of corneal endothelial dysfunction.[23]

The current study found a mean CV% of 32.3% ± 3.7, similar to previous studies from Egyptian,[6] Turkish,[12] and Chinese[8] populations, furthermore, it was lower than Nigerian[16] and higher than Iranian populations.[17]

CV% demonstrated significant gender differences where males had higher CV% than females ($p < 0.01$) which goes in line with the Egyptian study,[6] nevertheless researchers from Iranian,[17] Turkish,[12] and Filipino[19] populations reported no significant gender differences in CV%.

CV% showed a significant moderate positive ($r = 0.35$) correlation with age, which was consistent with many previous researches.[6,12,17]

Hexagonality

The mean percentage of the hexagonal cell was 52.8% ± 9.6. This was similar to the Egyptian[6] and Turkish[12] populations, but higher than the Nigerian[16] and Caucasian[9] populations.

Hex (%) in our study exhibited significant gender differences ($p < 0.01$), similar to previous research.[6,24] Abdellah et al linked this gender difference to the smoking effect as males smoke more than females.[6] Other research revealed the effect of smoking on hexagonally.[25] Meanwhile, reports indicate that there are no gender disparities in Hex (%).[9] In the current study, Hex (%) decreased with aging ($r = -0.31$) similar to earlier studies.[6,8,9,12,19]

The variable morphology and density of endothelial cells among different ethnic groups, as indicated above, highlight the significance of the current work in establishing normative Libyan data.

Limitations of the Study

The small sample for subgroup analysis limited this study as well as missing information about the corneal diameter and its effect on corneal endothelial cell density.

Recommendation

We recommend another study in the future with a larger number of participants, the use of another instrument model, and to measure the corneal diameter to validate our findings.

Conclusion

The CCT, MCD, and Hex (%) decrease while the CV% increases with age, there was no statistical difference in the CCT and MCD between males and females, whereas CV% and Hex (%) demonstrated significant gender differences.

Conflict of Interest
None declared.

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