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Corneal Endothelial Changes among High Myopic Patients of Different Age Groups

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ABSTRACT

Background: Myopia a refractive error that is a major contributor to visual disability across combined age groups all over the world.

Aim of the work: To detect changes in the corneal endothelial cells parameters among high myopic patients versus emmetropic individuals in different age groups aiming at proper identification of the endothelial cells behavior; hence we can predict more precise results after phaco refractive surgeries and implantable collamer lens (Icl) implantation**.**

Patients and methods: This case-control research, performed on 168 eyes of 84 participants allocated into two groups: Group I (42 cases, 84 eyes): individuals with high myopic eyes, and Group II (42 cases, 84 eyes): individuals with healthy emmetropic eyes as a control group at Outpatient Clinic, Ophthalmology Department, Suez Canal University Hospital, Ismailia, Egypt for a period of six months from February 2021 to July 2021. (NIDEK CEM-530) specular microscope was utilized to determine the central corneal thickness (CCT) of the participants.

Results: The study observed no significant variance in CoV% among high myopic and emmetropic eyes, but there was a significant variation in ECD (Endothelial Cell Density) and HEX% (Hexagonality) among the two groups. The mean ECD in high myopic eyes was 2533.79±315.37 cells/mm^2, while in emmetropic individuals, it was 2706.65±313.50 cells/mm^2.

Conclusion: The research found that corneal endothelial cell density and morphology significantly vary among different age groups, indicating a significant effect of age on corneal endothelial function.

Keywords: Cornea, Endothelial Changes, Myopia, Icl implantation.

INTRODUCTION

Myopia a refractive error that is a prominent factor contributing to visual disability across combined age groups all over the world. The condition has variable prevalence according to geographical region, age and race, with particularly high prevalence in East Asian countries, but affects both the developed and the developing world [1,2].

The cornea is a transparent structure that constitutes the anterior 1/6 of the outer coat of the eye globe and has the dual function of protection and refraction as it represents two third of the refractive power of the eye. The human cornea is typically described in five layers: an overlying epithelium, a fibrous network underneath the epithelium called Bowman's layer, the majority of the thickness (90%) constituted by the stroma which is composed of regularly arranged collaged fibers in an extracellular matrix and scarce cells, and a Descemet's membrane which acts as the basement membrane of the single-layered corneal endothelial cells - the final layer of the cornea [3, 4]. The discovery of Dua's layer, which is an acellular pre-Descemet's space has led to the revision of corneal layers and their re-arrangement into six layers instead of five [5].

The corneal endothelial cell layer involves a single layer of non-regenerating hexagonal cells that covers the posterior surface of Decrement's membrane in direct contact with the anterior chamber of the eye. The cells exhibit metabolic activity and have a crucial function in preserving transparency by actively transporting water from the stroma to the aqueous, hence maintaining a partly dehydrated condition with 70% water content [6,7].

Non-contact specular microscope is a non-invasive method used to analyze the corneal endothelial cells quantitatively and qualitatively, with accurate and reliable measurements of mean cell density, coefficient of variation in the cell size, in addition to hexagonality index. These parameters provide a reflection of the anatomical and functional status of the corneal endothelium [8-10].

This research was designed to detect changes in the corneal endothelial cells' parameters among high myopic patients versus emmetropic individuals in different age groups aiming at proper identification of the endothelial cells' behavior.

PATIENTS AND METHODS

This was case-control research, done at Outpatient Clinic, Ophthalmology Department, Suez Canal University Hospital, Ismailia, Egypt for a period of six months from February 2021 to July 2021. A total of 168 eyes of 84 individuals were enrolled, they were allocated into two groups: **Group I** (42 cases, 84 eyes): individuals with high myopic eyes, with mean age of 39.02 ± 11.75 included (Group A (Age 18 - 35), Group B (Age 35 - 55) and Group C (Age > 55) and **Group II** (42 cases, 84 eyes): individuals with healthy emmetropic eyes as a control group, with mean age of 35.31 ± 18.17 included (Group A (Age 18 - 35), Group B (Age 35 - 55) and Group C (Age > 55))

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Inclusion criteria: Both sexes (male and female), patients' age ≥18 years, myopia ≥ - 6 diopters and clear cornea with the absence of any other ocular disease**.**

Exclusion criteria: Patients with pre-existing corneal disease e.g. corneal dystrophy, scar or corneal ulcers, Co-existing ocular diseases, e.g., glaucoma or uveitis, systemic diseases affecting ocular tissue e.g. DM, previous eye surgery or ocular trauma, any ocular immune diseases, e.g., Behcet and any systemic immune diseases, e.g., SLE.

Methods:

Enrolled patients were evaluated by: Complete history taking and ophthalmic and fundus examination. Uncorrected visual acuity (UCVA) and best corrected visual acuity (BCVA) were measured using Landolt's chart. Fundus examination was measured by: Indirect ophthalmoscope (TOPCON ID-5) and Volk's non-contact double aspheric biconvex lens (power: + 90).

Specular microscope procedure

A non-contact specular microscope: (NIDEK CEM-530):

The morphology and cell count of corneal endothelium were assessed utilizing a noncontact specular microscope. The endothelium of the cornea may be studied and seen with the help of a non-invasive photography method called specular microscopy. For specular microscopy, the individual was sat with his chin on the chin rest and his forehead gently pressed against the headband, and he was instructed to stare into the built-in fixation target. The head position was adjusted, and automated focusing was performed such that the image of the pupil on the monitor was clearly focused and inside the targeting circle shown on the screen. The instrument illuminates the cornea and records the picture that is reflected from the boundary among the corneal endothelium & the aqueous humor. The gadget examined the reflected picture and presented it as a specular photomicrograph. Specular microscopy enables the assessment of endothelial cell count, cell density, polymegathism (varying in size), and pleomorphism (change in form). The measurements were obtained using the center technique. The equipment successfully captured specular microscope images and measured corneal thickness when properly aligned and focused. Specular microscopy is the most accurate method for examining the corneal endothelium in clinical practice. In this study we used (NIDEK CEM-530) specular microscope, it is provided with a built- in Pachymetry to measure central corneal thickness (CCT) at each central, paracentral and peripheral points. The Paracentral Image Capture Function of the CEM-530 is distinct from that of conventional central and peripheral specular microscopy. Enhancing the evaluation of the region encircling the central image, the paracentral images were captured at eight sites at a 5º visual angle within a 0.25 mm x 0.55 mm field. Using the diagnostic information provided by the paracentral images, the central endothelial images can assess endothelial cells with greater precision. The CEM-530 specular microscope collects a total of 16 images, which are then sorted automatically according to their quality. The image with the highest quality, which is most suitable for study, is highlighted in orange. After selecting the image, the computer automatically assesses, computes, and presents the average cell density (cells/mm2), coefficient of variation (CV%) in cell size, and percentage of hexagonal cells (HEX%).

Ethical Considerations: The patient provided written informed permission to participate in the trial. Permission to conduct the study was received from the Ophthalmology Department at Suez Canal University Hospitals, in addition to clearance from the Research Ethics Committee of the Faculty of Medicine in Suez Canal university. For the purpose of conducting research involving human subjects, this study has been carried out in conformity with the Declaration of Helsinki, which is the Code of Ethics of the World Medical Association.

Statistical Analysis

Statistical Package for Social Science (SPSS) version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA) was utilized in order to collect, tabulate, and perform statistical analysis on the data that was acquired. Using the Shapiro-Wilk test, the data were examined to determine whether or not they were normal. The quantitative data were represented as the mean plus or minus the standard deviation (SD) and the range, while the qualitative data was converted into numerical values and percentages. The chi-square test ($\chi 2$) was applied to assess the statistical disparity between qualitative data. The statistical distinction among quantitative data in two groups, namely emmetropic eyes (GI) and high myopic eyes (GII), was assessed utilizing the Independent T test for parametric variables and the Mann Whitney test for non-parametric variables. All statistical comparisons were conducted utilizing a two-tailed test with a significance level determined by p-value. A p-value above 0.05 indicates non-significance, a p-value below 0.05 indicates significance, and a p-value under 0.001 indicates high significance.

RESULTS

Table (1): Demographic data of the two examined groups:

		Myopic	Emmetrope
		N of patients = 42	**N of patients = 42**
Age	Mean±SD	39.02 ± 11.75	35.31 ± 18.17
	Range	18 – 60	19 - 73
	18 – 35 yrs	30 eyes (35.7%)	52 eyes (61.9%)
	35 – 55 yrs	42 eyes (50.0%)	20 eyes (23.8%)
	> 55 yrs	12 eyes (14.3%)	12 eyes (14.3%)
Sex	Female	25 (59.5%)	30 (71.4%)
	Male	17 (40.5%)	12 (28.6%)

The mean ± SD age of myopic cases was 39.02 ± 11.75 years and of emmetropic cases was 35.31 ± 18.17 years. Regarding age groups, half cases (50%) were 35 – 55 years in myopic group and 52 (61.9%) were 18 – 35 years in emmetrope group. In myopic group, male to female ratio was 0.68: 1, meanwhile in the emmetrope group, male to female ratio of 0.40:1 (Table 1).

There was significant variance observed among myopic individuals and emmetropic ones in age of 18-35 years concerning HEX% and ECD; while there was no significant variance among the two groups concerning CV% (Table 2).

Table (2**):** Comparison between myopic patients and emmetropes regarding corneal endothelial parameters in age 18-35 years.

Group A (18 –35 yrs)		**myopic Group I**	**Emmetrope Group II**	**Test value•**	**P-value**	**Sig.**
		N of eyes = 30	**N of eyes = 52**			
HEX%	Mean±SD Range	63.40 ± 10.79 41 – 77	72.12 ± 4.02 64 – 77	-5.247	0.000	HS
CV%	Mean±SD Range	29.83 ± 5.28 24 – 42	29.25 ± 5.74 23 – 42	0.456	0.649	NS
CD	Mean±SD Range	2574.23 ± 423.52 2018 – 3217	2789.17 ± 333.40 2273 – 3591	-2.543	0.013	S

• ***t:*** *Independent T test*

There was significant variance detected amongst the two examined groups in age of 35-55 years concerning CD while there was no significant variance among the two investigated groups concerning Hex% and CV% of cell size (Table 3)

Table (3): Comparison between myopic individual and emmetropic ones regarding corneal endothelial parameters in age 36-55 years

Group B (36 –55 yrs)		**Myopic Group I**	**Emmetrope Group II**	**Test value•**	**P-value**	**Sig.**
		N of eyes = 42	**N of eyes = 20**			
HEX %	Mean±SD Range	66.55 ± 9.93 42 – 75	65.45 ± 8.08 54 – 77	0.431	0.668	NS
CV%	Mean±SD Range	27.86 ± 4.02 22 – 36	29.65 ± 3.57 22 – 34	-1.699	0.095	NS
CD	Mean±SD Range	2533.79 ± 315.37 2018 – 3217	2706.65 ± 313.50 2273 – 3221	-2.021	0.048	S

There was significant variance detected between the two investigated groups in age of**> 55 yrs** years concerning HEX%; while there was no significant variance among the two examined groups concerning CV% of cell size and ECD (Table 4).

Table (4): Comparison among myopic individual and emmetropic ones concerning corneal endothelial parameters in age >55 years

Group (>55 yrs)	C	Myopic Group I	Emmetrope Group II	Test value•	P-value	Sig.
		N of eyes = 12	N of eyes = 12			
HEX %	Mean±SD Range	67.25 ± 3.93 63 – 71	58.75 ± 12.32 41 – 69	2.276	0.033	S
CV%	Mean±SD Range	26.75 ± 2.99 23 – 30	26.67 ± 2.96 23 – 31	0.069	0.946	NS
CD	Mean±SD Range	2646.08 ± 267.07 2140 – 2865	2431.67 ± 326.56 2087 – 3075	1.761	0.092	NS

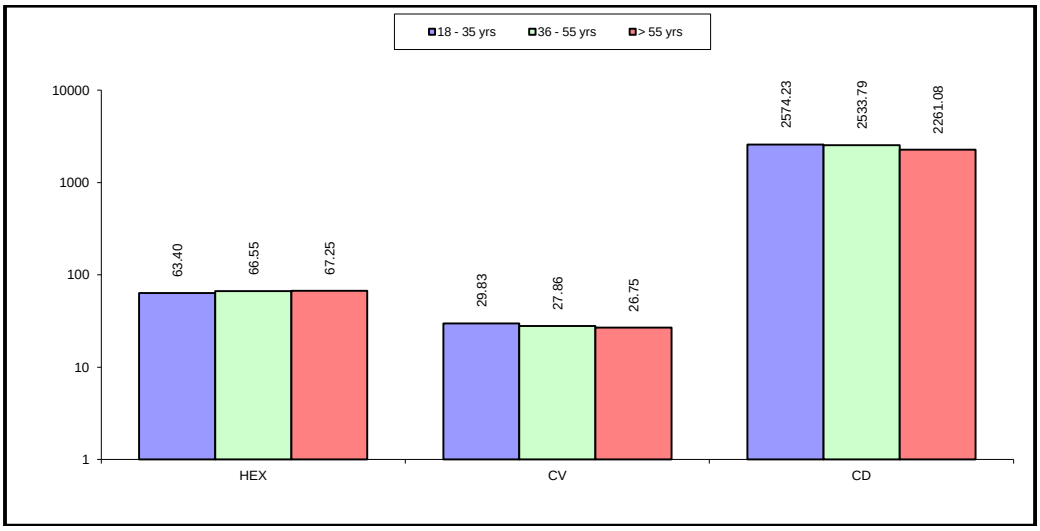

Fig. (2): Comparison among the three age groups in myopic patients concerning corneal endothelial parameters.

There was significant variance between the three age groups in emmetrope group concerning HEX% and ECD; while there was no significant variance detected among the three age groups concerning CV%. It was found that there was no statistically significant distinction among age of 18-35 years and age of 36-55 years concerning ECD, while there was statistically significant variance among both ages and the age > 55 concerning ECD. Also, there was statistically significant variance amongst 18-35 vs 36-55 yrs, 18-35 vs > 55 yrs and 36-55 vs > 55 yrs concerning HEX (Table 5).

Table (5): Comparison between the three age groups concerning corneal endothelial parameters in emmetropes patients

Emmetropes Group II		Group A (18 - 35 yrs)	Group B (36 - 55 yrs)	Group C (> 55 yrs)	Test value•	P-value	Sig.
		N of eyes = 52	N of eyes = 20	N of eyes = 12			
HEX%	Mean±SD Range	72.12 ± 4.02 64 – 77	65.45 ± 8.08 54 – 77	58.75 ± 12.32 41 – 69	21.759	**<0.001**	**HS**
CV%	Mean±SD Range	29.25 ± 5.74 23 – 42	29.65 ± 3.57 22 – 34	26.67 ± 2.96 23 – 31	1.546	0.219	NS
CD	Mean±SD Range	2789.17 ± 333.40 2273 – 3591	2706.65 ± 313.50 2273 – 3221	2431.67 ± 326.56 2087 – 3075	5.812	**0.004**	**HS**

Post hoc analysis utilizing LSD test			
Parameters	**P1**	**P2**	**P3**
HEX	<0.001	<0.001	0.008
CD	0.342	0.001	0.024

P1: between Group A and Group B **p2: between Group A and Group C** **P3: Group B and GroupC**

DISCUSSION

According to age, all participants of the two groups were further divided into 3 sub-groups 18 - 35-year (group A), 35 - 55-year (group B), > 55-year (group C); each of them included 30 (35.7 %), 42 (50 %), 12 (14.3 %) myopic eyes and 52 (61.9 %), 20 (23.8%), 12 (14.3 %) emmetropic eyes, respectively. In myopic eye group, there were 17 (40.5%) males and 25 (59.5%) were females with male to female ratio of 0.68: 1, meanwhile in emmetropic eye group, there were 12 (28.6%) males and 30 (71.4%) were females with male to female ratio of 0.40:1. Three aspects of corneal endothelial morphology, involving ECD, the CoV, and the % HEX were assessed using non-contact specular microscopy.

Our results revealed that the mean ECD in 18-35 aged individuals with high myopic eyes (group A) was 2574.23 ± 423.52 cells /mm^2, which was less than emmetropic individuals (control group) with mean ECD of 2789.17 ± 333.40 cells /mm^2. There was a significant variance among high myopic and control group concerning ECD (p=0.013). These finding were in line accordance with that reported early with [11].

Also, in agreement with that, **Kumar *et al.*** [12] concluded that the degree of myopia is subjectively related to the percentage of hexagonal appearance of corneal endothelial cells and the variations in cell density**.**

Sanchis-Gimeno *et al*. contrary to our results, stated no statistically significant distinctions (P=0.404) in corneal endothelial cell density among emmetropic and myopic eyes [13]**.**

Regarding CoV %, Our findings demonstrated that the mean of CoV% in high myopic eyes (18-35 aged group A) was 29.83 ± 5.28, while in emmetropic group, it was 29.25 ± 5.74. There was no significant distinction among the two groups concerning CoV%.

Our results revealed that the mean HEX % in 18-35 aged individuals (group A) with high myopic eyes were 63.40 ± 10.79, which was less than emmetropic individuals with mean HEX % 72.12 ± 4.02. There was a significant variance among high myopic and control group regarding HEX % (p=0.001).

These findings were in line with other earlier studies [12,14]**,** who concluded that variations in the proportion of corneal endothelial cells exhibiting a hexagonal morphology are subjectively proportional to the degree of myopia. The decrease of HEX cells percent in myopic group compared to emmetropic healthy group could be explained on the basis that, since corneal endothelial cells must flatten in order to conquer the expanded surface, it's possible that the likelihood of polymorphism rises, and the percent of hexagonal cells falls [14].

Our result revealed that the mean ECD in 35-55 aged individuals with high myopic eyes (group I) was 2533.79±315.37 cells/mm^2, which was less than emmetropic individuals (control group) with mean ECD of 2706.65±313.50 cells/mm^2. There was significant variance among high myopic group individuals and emmetropic individuals regarding ECD (p = 0.048).

These findings were in accordance with an earlier study [11] and also in agreement with that demonstrated by **Kumar *et al.*** [12], who concluded that the degree of myopia is subjectively determined by variations in the density of corneal endothelial cells and the proportion of cells that exhibit a hexagonal appearance; while our findings in contrast to these studies regarding the percentage of hexagonal appearance of the cells, as our results revealed that there was no statistically significant variance among the two studied groups concerning HEX%, this may be due to selection of patients with low and moderate myopia in those studies .

In > 55 years aged individuals, our results revealed that there was significant variance found among the two investigated groups concerning HEX%, (P= 0.033), mean HEX % in myopic individuals (group I) was 67.25±3.93, which was higher than mean HEX% in emmetropic individuals (group II) 58.72±12.32.

This conclusion needs to be explained more by doing further studies using a large sector of participants, as there were no previous researches proved these results before.

In > 55 years aged individuals, our results discovered that there was no statistically significant variance among the two examined groups concerning CoV% of cell size and ECD.

These findings are in contrast with **Delshad and Chun** [11] and **Kumar *et al.*** [12], who concluded that variations in the proportion of corneal endothelial cells exhibiting a hexagonal morphology are subjectively proportional to the degree of myopia.

Regarding the association among the three age groups and corneal endothelial parameters in myopic individuals (group I), we found that there was a non-significant variance among the three age groups concerning HEX% and CoV%; while there was statistically significant variance was found regarding ECD (p=0.029). In contrast, there was a non-significant distinction among 18-35 age group (A) vs 36-55 years (B) regarding ECD.

Our results demonstrated that in a healthy emmetropic individuals, there was an age-related progressive decrease in specular parameters, with a highly significant difference among different age groups concerning HEX, and ECD, p < 0.005, without significant variance amongst three age groups concerning CoV %. Also, our findings revealed that there was a non-significant difference among 18-35 group (A) vs 36-55 years (B) regarding ECD.

Our results are in line with that reported with **Rao *et al.*** [15], who demonstrated that in a normal healthy adult Pakistani population, there was a progressive decline in CED and hexagonality of corneal endothelial cells with age, while COV and average cell size were elevated.

Also, our results were along with **Islam *et al*.** results, who compared the corneal endothelial cell density and morphology in 464 eyes of 232 healthy Pakistani cases with ages among 10 & 80 years of either gender using Topcon SP3000P non- contact specular microscopy. They revealed that the mean CD and hexagonality of the cell were significantly decreased with increasing age ((r = 0.497) and (r = 0.397, correspondingly **[16].**

Contrary to our finding, there are no variances in corneal endothelial cell density among emmetropic, myopic, and hyperopic subjects according to **Sanchis-Gimeno *et al***. They investigated the differences in the mean of three consecutive measurements of corneal endothelial cell density in 30 emmetropic (average age of 27.3 ± 4.0 years old), 30 myopic (26.6±4.1 years old) and 30 hyperopic (26.8 ± 4.4 years old) subjects using Topcon SP-2000P noncontact specular microscope, and they noted that the mean of ECD was 3076, 3048, 3033 cells/mm^2 in emmetropic, myopic and hyperopic eyes correspondingly **[13].**

CONCLUSION

We concluded that visible information regarding the function of the cornea can be obtained from the density and morphology of endothelial cells in the cornea. Vision with high myopia was characterized by a significantly reduced density and hexagonality of corneal endothelial cells in comparison to emmetropic vision. ECD (endothelial cell density) and morphology varied significantly among age groups, suggesting that age significantly influences the density and morphology of corneal endothelial cells.

DECLARATIONS:

- **Consent for publication:** I confirm that every author has given their consent to submit the work.
- **Availability of data and material:** Available
- **Competing interests:** None
- **Funding:** No fund
- **Conflicts of interest:** no conflicts of interest.

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