ORIGINAL ARTICLE

# Age Related Changes in Normal Corneal Endothelium Using Specular Microscope

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## ABSTRACT

**Objective:** To evaluate the changes in corneal endothelium with age in normal Pakistani population
**Methodology: A** descriptive cross sectional study was conducted in the Ophthalmology Department of the Helpers Eye Hospital, Quetta, Pakistan from March 12 to July 12, 2021. Two hundred eyes of 200 healthy subjects of both sexes between the ages of 20 to 70 years were recruited. Complete eye examination was done on each patient. Exclusion criteria included refractive error of >± 2.00 dioptres, corneal pathologies, glaucoma, uveitis, history of trauma, contact lens use, intraocular surgery, and diabetes mellitus. Corneal endothelial cell density (CED), mean cell area (MCA), coefficient of variation of cell size (CV) and hexagonality were analyzed by specular microscope (Shin-Nippon SPM-700; Rexxam Co.Ltd, Takamatsu, Japan). Pearson's correlation coefficient (r) demonstrated correlation between age and CED, CV, hexagonality and mean cell area.
**Results:** Mean age was 43.00±12.32 years. A total of 136 (68%) participants were male and 64 (32%) were female. Mean CED, average cell area, CV in cell size and hexagonality were 2705.91±235.70, 368.81±26.58, 41.97±10.77, and 47.37±6.67 respectively. Corneal endothelium parameters among age groups were statistically significant ($p< 0.01$). Pearson's correlation coefficient (r) revealed that CED (r= -0.755) and hexagonality (r= -0.709) decline while average cell area (r= 0.694) and CV of size (r=0.548) increase with age.
**Conclusion:** Our current study confirms the previous reports on relation of MCD, hexagonality, MCA, and CV with advancing age. The results of our study on endothelial cell in Pakistani population are beneficial for future researches.


**Key Words:** Corneal endothelium, corneal endothelial density, specular microscope.

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## INTRODUCTION

The corneal endothelium plays a vital role in the maintenance of corneal hydration, transparency and homeostasis and is an important part of the structure and function of the cornea[1]. The cornea is covered on its posterior surface by endothelium having hexagonal shape[2]. Any damage to corneal endothelium is irreversible as corneal endothelial cells (CECs) have limited proliferative capacity in vivo[3]. Cell density of 4000–5000 (cells/mm$^2$) is present at birth which declines with age by 0.3–0.6% per annum, with 2000–3000 cells/mm$^2$ in adults[4]. With aging, endothelial pump efficiency decreases, and the results of refractive surgery are not satisfactory[5]. Clinically, it is observed that cornea starts to decompensate when cell density is 400 to 600 cells/mm$^2$[2,6]. The variation in cell area is described by polymegathism. It is the coefficient of Variation (CV) determined by standard deviation cell area mean/cell area ìm$^2$. With rise in polymegathism, there is a decline in the precision of the average cell area[7]. The specular microscope allows a detailed examination of corneal endothelium, using a magnification which is many times greater than the slit lamp biomicroscopy[8]. It uses light beam on the corneal endothelium and reflected light rays are focused onto film plane on a monitor[9]. The noncontact nature of specular microscope is more tolerable for wider range of people[10].

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The objective of this study is to analyze morphological changes in corneal endothelium in normal subjects of Pakistani population. The rationale of the study is to generate evidence based data to help the practitioners in planning safest technique for intra-ocular surgeries and lasers and also to provide data for future researches.

The main aspect of the study is to analyze corneal endothelium in our population as it is crucial to assess endothelial health before surgeries, for impact of lasers during refractive procedures and assessment of donor cornea before corneal transplantation. Normative data regarding different aspects of eye is missing for Pakistani population, so it is the need of time to generate data that would be helpful in future researches.

## METHODOLOGY

This descriptive cross sectional study was conducted at the Ophthalmology Department, Helpers Eye Hospital, Quetta from March 12 to July 12, 2021 after approval from the Hospital Ethics Committee with reference No. HEHQ/246. The study was done according to the Declaration of Helsinki and using nonprobability consecutive sampling technique. Two hundred eyes from 200 subjects aged 20–70 years of either gender, either eye, refractive error of=± 2.00 dioptres, intraocular pressure of <± 21 mm hg, and normal cornea and fundus were enrolled in our study after taking written informed consent. All the participants had complete assessment of visual acuity, slit lamp bio microscopy for anterior segment examination with measurement of intraocular pressure, and fundoscopy. Subjects with refractive error of <± 2.00 dioptres, anterior segment disease such as corneal pathologies, glaucoma and uveitis, history of trauma, contact lens use, intraocular surgery, and diabetes mellitus were excluded. All subjects were stratified into five age groups (21–30 years, 31–40 years, 41–50 years, 51–60 years, and 61–70 years). Corneal endothelial parameters were assessed using specular microscope (Shin-Nippon SPM–700; Rexxam Co.Ltd, Takamatsu, Japan) that included corneal endothelial cell density (CED), mean cell area, hexagonality, and coefficient of variation of cell size (CV). Specular microscopy was performed by single examiner between 9:00 AM and 1:00 PM. All subjects were asked to fixate after head positioning and three images from cornea were obtained. The mean of three readings was taken for analysis: technique with 95 percent confidence interval; margin of error 10 percent.

Data was analyzed using SPSS version 23. Frequency and percentage for qualitative data such as gender was calculated. Mean and standard deviation for variables including age and corneal endothelial cell density (CED), average cell area, coefficient of variation of cell size (CV) and hexagonality was calculated. Correlation of corneal endothelial parameters (CED, hexagonality, CV, mean cell area) with age was evaluated by Pearson's correlation coefficient (r). Strong correlation was indicated by r > 0.7. A p value of <0.05 was considered significant.

## RESULTS

Two hundred healthy subjects aged 20–70 years (mean age 43.00±12.32 years) were enrolled in the study. Total 136 (68%) were male and 64 (32%) were female. Mean corneal endothelial cell density was 2705.91±235.70. The mean cell area was 368.81±26.58. Mean coefficient of variation in cell size and hexagonality was 41.97±10.77 and 47.37±6.67 respectively. Corneal endothelial characteristics among different age groups are given in Table 1. Positive relationship of age was found with cell area (r =± 0.694, p<0.01) and coefficient of variation of size (r=0.548, p<0.01), while CED (r= -0.755, p<0.01) and hexagonality (r= -0.709, p<0.01) decreased significantly with age (Table 1).

**Table I: Corneal Endothelium Parameters According to Age (p <0.01)**

| Age group (years) | Age (years) | CED (cells/mm$^2$) | Average Cell Area (μm$^2$) | CV in Size (%) | Hexagonality (%) |
|---|---|---|---|---|---|
| 20–30 | 23.00 ± 1.01 | 3063.50 ± 198.31 | 327.75 ± 21.24 | 32.00 ± 3.04 | 54.75 ± 2.20 |
| 31–40 | 37.75 ± 2.29 | 2714.88 ± 159.92 | 369.62 ± 25.59 | 41.00 ± 10.37 | 48.37 ± 5.78 |
| 41–50 | 47.25 ± 1.93 | 2681.25 ± 105.71 | 373.63 ± 14.77 | 41.75 ± 10.20 | 47.25 ± 5.39 |
| 51–60 | 54.41 ± 2.80 | 2506.29 ± 106.87 | 390.47 ± 3.50 | 48.12 ± 9.94 | 44.71 ± 1.57 |
| 61–70 | 65.22 ± 3.26 | 2399.57 ± 129.06 | 394.26 ± 9.84 | 54.65 ± 3.77 | 36.57 ± 2.39 |
| Mean | 43.00 ±12.32 | 2705.91 ± 235.70 | 368.81 ± 26.58 | 41.97 ± 10.77 | 47.37 ± 6.67 |
| Pearson Correlation | – | -0.755 | 0.694 | 0.548 | -0.709 |

## DISCUSSION

Morphology of single layer of hexagonal cells of corneal endothelium is very important to maintain the clarity and transparency of cornea, by its ionic pumping and barrier function to help the stroma to be in a partially dehydrated state. Studies have shown that genetical, racial, environmental factors, and age affect endothelial integrity[11,12]. According to literature, a decrease in ECD was observed in Portugal's population at a rate of 5-6% per year[13]. Other risk factors related to endothelial loss were studied by different researchers who stated that Fuchs endothelial dystrophy is one of the leading causes of nonfunctioning corneal endothelium in the West, while in Asian countries endothelial dysfunctions are commonly iatrogenic injuries or other factors such as pseudoexfoliation syndrome[14,15].

Reduced corneal endothelial density can lead to corneal decompensation, if that is below 500 cells/mm$^2$[,6,15]. Several studies show the interrelation of corneal cell density with age, ethnicity, gender, and race, and provide research based evidence that endothelial morphologic changes do exist among different racial, ethnic, and age groups[6, 8,16,17]. Therefore, it is highly valuable to build up the normative data on endothelial function for different races and ages, based on which future researches and plans can be made.

We have conducted this study to collect data about endothelial cell properties in Pakistani population because very limited data is available of our local population's corneal endothelium characteristics. In our study, we observed that with increasing age there is a decrease in mean corneal endothelial density, and hexagonality of endothelial cells, increase in MCA, increased CV in cell size. In our study, we observed mean corneal endothelial density 2705.91±235.70 in our healthy population, and same trend is reported in Turkish population[5]. The reason of cell loss with age is not clear; it is assumed that it may be due to high metabolic destruction of endothelial cells with increasing age[6].

MCA, CV, and hexagonality are also related with MCED. The mean cell area in our study was 368.81±26.58. Mean coefficient of variation of cell size and hexagonality was 41.97±10.77 and 47.37±6.67 respectively. Such variations were also noticed by Nigerian researchers and they mentioned the MCD of 2610.26±371.87 cells/mm$^2$ with reducing hexagonality of 46.52±8.83%, MCA 392.22±68.03µm, CV 43.95±9.50%[18]. Similar variations in corneal endothelial cells properties have been observed by many international researchers that endorse our results[18,19]. It was noted that American and Japanese populations have a decline in MCD but at a lower rate than Turkish population, while Iranian and Indian populations have a higher rate of MCD decline with advancing age[6,16,17]. So, there is a general trend towards low cell count with increasing age[18].

# CONCLUSION

Our study confirms the previous reports that MCD declines with advancing age and it correlates with the decrease in the percentage of hexagonal cells, and increase in CV in cell size and MCA with advancing age. The results of our study on endothelial cell are beneficial in Pakistani population for future researches. Normal corneal endothelium is required for good visual outcome in refractive and other intraocular surgery and to understand corneal pathologies. Knowing the normal endothelial cell count and changes related to age within local Pakistani population would help to plan the safe surgical approaches and techniques to prevent further loss, as its function decreases with age due to metabolic destruction of endothelial cells and reduced pump function.

**Conflict of interest:** The authors declare no conflict of interest.

**Authors' Contribution:** MW and MM: Conceived the idea, worked on data interpretation, manuscript writing and final approval; UP and CT: Worked on data analysis, drafting of manuscript and critical review.

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