# Age-related changes of the corneal endothelium in a Hispanic elderly population.

**J Valdez-Garcia** ( jorge.valdez@itesm.mx )
Instituto Tecnologico y de Estudios Superiores de Monterrey

**Gustavo Ortiz-Morales**
Instituto Tecnologico y de Estudios Superiores de Monterrey

**Nallely Morales-Mancillas**
Instituto Tecnologico y de Estudios Superiores de Monterrey

**Jorge Luis Domene-Hickman**
Instituto Tecnologico y de Estudios Superiores de Monterrey

**Julio Hernandez-Camarena**
Instituto Tecnologico y de Estudios Superiores de Monterrey

**Denise Loya-Garcia**
Instituto Tecnologico y de Estudios Superiores de Monterrey

**Judith Zavala**
Instituto Tecnologico y de Estudios Superiores de Monterrey

**Alejandro Rodriguez-Garcia**
Instituto Tecnologico y de Estudios Superiores de Monterrey

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# Abstract

**Purpose**: To assess the corneal endothelial morphometry in healthy elderly Hispanic eyes.

**Methods**: A retrospective, cross-sectional, observational, descriptive, and analytical study was designed to assess by specular microscopy the central region of the corneal endothelium. In a 4-year period, a total of 75 eyes from 42 patients were studied. All eyes included were from patients 65 or older (mean: 73.87±6.86), without ocular disease or surgeries.

**Results**: The mean cell density (MCD) was 2268±597.0 cells/mm$^2$. 44% of patients had polymegethism, with an average coefficient of variation (CV) of 42.04 ± 10.1%. 76% of patients had low pleomorphism, with an average of 42.3 ± 8.9% hexagonal cells. The mean corneal thickness was 537±38.2 µm. There was no statistically significant difference between age groups for MCD, CV, hexagonality and pachymetry (p=>.05). 27% of patients had corneal guttata.

**Conclusion**: This study suggests that the elderly Hispanic population has a high prevalence of polymegethism, pleomorphism and guttata. Surprisingly, the oldest age group (>85) had an above average MCD, low polymegethism and good pleomorphism.


# Introduction

The corneal endothelium is an essential part of the structure and function of the cornea playing a key role in the maintenance of corneal hydration homeostasis and transparency.

The measurement of central corneal thickness (CCT), endothelial cell density, size, and morphology is essential for evaluating the endothelial cell function for diagnostic purposes and the preoperative evaluation of any anterior segment surgery[1]. The total number of endothelial cells may be affected by aging, trauma, UV exposure, inflammation, and surgery, among others. [2–5]

Corneal endothelial cell alterations may affect corneal transparency, worsening visual outcome. Age plays an essential role in this process since it has demonstrated a direct correlation with endothelial cell loss by reducing pump functionality and corneal wound-healing, which contribute to reduced visual acuity [5, 6].

Various studies performed in diverse populations analyzing the corneal endothelial cell density highlight the importance of including the endothelial cell morphology in correlation to ethnicity and age. Available data form these studies show statistically significant differences in endothelial cell parameters among ethnic groups and sexes. [1, 7–14]

The differences in endothelial cell morphology among ethnic groups, age and sex show that normative data on the endothelial cell parameters may help assess the endothelial cell function in individual patients and could even further our understanding in corneal endothelial diseases.

The purpose of the present study is to describe the cell density and morphologic characteristics of the corneal endothelium of a healthy elderly Hispanic population.

## Subjects And Methods

A retrospective, cross-sectional, observational, descriptive, and analytical study was designed to study the specular microscopy characteristics of the corneal endothelium from elderly Hispanic patients. The study was conducted at the Tecnologico de Monterrey Institute of Ophthalmology and Visual Sciences between 2013 and 2017. All patients enrolled for the study participated voluntarily in the study after reading and signing an informed consent previously reviewed and approved by the Ethics and Research Committees (#ARCC/ECH2019) of our institution following the tenets of the Declaration of Helsinki.

Inclusion criteria comprised patients over 65 years of age who came for a routine ophthalmological examination and where otherwise healthy. Exclusion criteria included a past medical history of ocular trauma, corneal or intraocular inflammation, use of systemic drugs that could affect endothelial cells, evidence of endothelial disease during slit lamp examination, previous ocular surgery, increased intraocular pressure, corneal opacity, or retinal photocoagulation procedures.

After a complete medical history and general ophthalmologic examination, all eyes of patients included for the study had specular microscopy (SM) performed by the same technician (SIS), using the EM-3000 specular microscope (Tomey®, Phoenix, AZ, USA) at similar room temperature and humidity conditions. EM-3000 is a non-contact specular microscope that uses a charge-coupled device camera to capture 15 images in series, it automatically selects and displays the finest among these images. The in-built software allows for fast and precise analysis of endothelial parameters. A wide range capturing area of 0.25 × 0.54 mm allows a larger count of cells. Corneal thickness measurement accuracy is +/- 10 µm.

Only the central corneal measurement point was considered for analysis. Parameters studied included the mean endothelial cell density (MCD), the mean cell area (MCA), the coefficient of variation (CV) of cell area (calculated as SD/mean cell area in µm), the percentage of hexagonal cells (PHC), and the CCT. Polymegethism was considered as a CV over 40% and pleomorphism when less than 50% of the endothelial cells showed hexagonality. SM images were classified as healthy when minor dark spots were present or as having guttae, which are mound-shaped excrescences in the Descemet´s membrane.

Patients were classified according to age into five groups: 65–69, 70–74, 75–79, 80–84 and ≥ 85 years old. All statistical analyses were performed using STATA v. 12.0 (StataCorp® LLC, Texas, USA). Continuous data are presented in mean ± SD and categorical data as proportions. A two-tailed unpaired t-student test was performed to compare cell parameters according to gender. A two-way analysis of variance was performed between age groups for the values of CCT and CV and Kruskal-Wallis test for the rest of the parameters studied, since they showed a non-normal distribution. Multiple regression analysis was conducted to determine the change in endothelial cell density with age, CV, MCA, PHC, and CCT. A P value less than 0.05 was considered statistically significant.

This study considered a small size sample from a local population. Given the retrospective descriptive nature of this study, statistic power calculation can no longer be applied, and if calculated considering the medium effect size obtained from the sample (0.3), it is low. [15–17] The confidence interval considered in our analyses was 95%, which supports the findings.

## Results

A total of 75 eyes from 42 patients corresponding to 22 (52.38%) males and 20 (47.61%) females over 65 years old were studied. An average number of 207 ± 83.86 (95% CI 188 to 226) endothelial cells were counted. The endothelial cell density and morphology according to patients age distribution are shown in table 1. The endothelial cell parameters and CCT according to gender are shown in Table 2.

# Mean cell density.

The MCD across all age groups was of 2268 ± 597.0 cells/$mm^2$ (95% CI 2130 to 2400). A small decline was observed as age increased, except for the ≥85 years group, where surprisingly an increase in cell density was observed. These changes in MCD among age groups were not statistically significant (p= 0.27, fig.1). Nine patients (12%) had a CD over 2800 cells/$mm^2$, while 17 eyes had less than 2000 cells/$mm^2$; of those, 13 (17%) had fewer than 1500 cells/$mm^2$.

# Mean cell area.

The MCA across all age groups was 488 ± 191.3$\mu m^2$ (95% CI 445 to 531) No statistically significant difference in MCA was observed among age groups (p=0.18) Although a steady increase with age was recognized, this was not statistically significant (R=0.02,p= 0.44, fig.2).

# Mean coefficient of variation.

The MCV for all age groups was 42.04 ± 10.1% ( 95% CI 39.8 to 44.3). No statistical difference was observed among groups for MCV (*p*=0.21, fig.3). The 65-69 years group had the highest prevalence of polymegethism, while the ≥85 years group had the lowest (52% of patient *vs.* 33%, respectively). The latter also showed the lowest MCV of all age groups (36.8%).

# Mean hexagonality.

The PHC was 42.3 ± 8.9% (95% CI 40.3 to 44.3)No statistical difference was observed among groups for PHC (*p=* 0.42*)*. The 80-84 years group had the lowest PHC, while the ≥85 years group had the highest (38.3% *vs.* 46.6%, respectively). Age was not found to be a risk factor for pleomorphism (R=0.001,

*p*=0.75) in this population. The 75-79 years group had the highest prevalence of pleomorphism (92%) while the ≥85 years group had the lowest (45%).

# Mean central corneal thickness.

The mean CCT for all age groups was 537 ± 38.2µm (95% CI 528 to 546). A steady increase in CCT with age was observed (R=0.056, *p*=0.04, fig.4). No statistical difference was noted among age groups for the mean CCT (*p*=0.35). The lowest mean CCT value was recognized in the 65-69 years group (525.0 ± 28.6µm).

Finally, a total of 20 eyes (27%) showed corneal guttata. A multiple regression analysis was run to predict cell density based on age, CV, MCA, PHC, and CCT: $F(5,69) = 154.29$, $p = <0.0001$, $R^2 = 0.9179$. From these variables, CV, MCA, and PHC added statistical significance to the prediction ($p=<0.05$).

## Discussion

It is important to distinguish between cornea guttata (primary and secondary), Fuchs endothelial dystrophy, and pseudo-exfoliation syndrome. Primary central cornea guttata is characterized by irregular excrescences of collagenous basement membrane material produced by endothelial cells in the central cornea. On the other hand, the secondary guttata is associated with trauma, degenerative corneal disease, and inflammation; it tends to disappear after the removal of the cause. [18, 19]

The primary central cornea guttata is classified as Stage 1 of Fuchs endothelial corneal dystrophy, some patients remain in this stage and never progress further. It may advance to the subsequent grades: Stage 2 (endothelial decompensation and stromal edema), Stage 3 (bullous keratopathy), and Stage 4 (avascular subepithelial fibrosis and scarring between the epithelium and Bowman's membrane). [5]

This entity differs from the pseudoexfoliation syndrome, in which small, white, and fluffy pseudoexfoliative deposits, are usually observed on the corneal endothelium, as well as, pigment deposition in the central cornea. In these patients, the damaged endothelium may cause corneal decompensation. This distinct endotheliopathy, may have been previously misdiagnosed as an "atypical non guttata Fuchs' endothelial dystrophy."[20]

Corneal endothelial cells are essential for maintaining corneal transparency by keeping the corneal stroma in a state of partial dehydration. Such homeostatic status is accomplished by a delicate balance between the rate of water entering the hydrophilic stroma through the endothelial barrier and its active removal by the action of the metabolic Na/K ATPase endothelial pump [21].

After birth, the corneal endothelial cell density (ECD) reaches its peak at approximately 6000 cells/$mm^2$ which starts to decline during the first years of life due initially to corneal growth [22]. Then, cell density continues its gradual decay over time, particularly between the ages of 20 to 80 years at an estimated

annual rate of 0.6% [6]. This slowly progressive cell loss is accompanied by a proportional increase in polymorphism and polymegethism [23].

When aging, toxicity, trauma, inflammation, or disease produce an ECD drop below 500 cells/mm$^2$, irreversible stromal edema occurs, and eventually the corneal loses its transparency [24]. For many years it was thought that corneal endothelial cells could not regenerate. However, recent investigations have shown that endothelial cells retain their capacity to divide and renew although they rarely do so [25]. A hypothesis that may help explain, at least in part such cellular behavior postulates that certain groups of dividing cells may enter a process of cellular senescence or replicative failure that limits their capacity to maintain their lifespan [26, 27] This hypothesis is supported by an age-related increase in the number of senescent cells in the human corneal endothelium [28–30]. Despite the relentless pursuit of a better understanding of the biologic mechanisms implicated in the gradual endothelial cell loss found during aging, there are still more questions than answers. Most probably, this phenomenon is multifactorial involving environmental, hormonal, biochemical and physiologic process related to aging [31].

There are several studies from diverse populations around the world analyzing the corneal endothelial cell density and morphology. Although investigators differ in their findings concerning the relationship between age and gender, and the corneal endothelial characteristics, the literature clearly shows a significant difference in corneal endothelial properties among races and ethnic groups [7–10].

In this study, MCD was found to be within normal values for healthy corneas [32]. Our mean number of cells studied per patient is higher than reported by other authors.

In table 3, the MCD among different elderly populations from different countries is portrayed. Although none of the authors studied exclusively elderly patients, a stratified calculation based on their age groups was performed. The MCD of 2268 cells/mm$^2$ found in our study across all age groups is very similar to the Caucasian population in Lithuania (2366 cells/mm$^2$) [1]. the Turkish population studied by Goktas et al. (2215 cells/mm$^2$) [11] and distant from the findings of Hashemian et al. [12] in Iran (1681.61 cells/mm$^2$) and also from Padilla et al. in the Philippines (2780.45cells/mm$^2$) [7].

It is of interest to mention the results of Graue et al. [13] and Molina et al. [14] in Mexican population from Central Mexico where patients in the 60 to 89 years group of age showed a MCD of 1805.33 cells/mm$^2$ and 1910.42 cells/mm$^2$ respectively, contrasting with our findings and suggesting that corneal endothelial cells characteristics may differ with our counterparts in the center and south of the country.

Another study in population from Central Mexico showed a MCD of 1909 cells/mm$^2$ in patients with a mean age of 71 years, interestingly, this cohort of patients had unilateral pseudophakic bullous keratopathy that developed after cataract surgery [33].

In our population, no difference was found in MCD as patients got older, suggesting that Hispanic patients who maintain ocular health after 65 years can also preserve a fair number of endothelial cells.

The latter is supported by the fact that 77% of patients had a cell density over 2000 cells/$mm^2$ and only 17% showed an MCD < 1500 cells/$mm^2$. It has been shown in previous reports that as the mean population studied increases, there is also an increased spread in the range of MCD counts, making the endothelial cell density measurement an unreliable index for the evaluation of corneal aging. The same finding applies to other animal species studied, like the dog, cat, monkey, and rabbit where the density and morphology of endothelial cells change with age, but the adult MCD remains constant [30, 31, 34].

As for the endothelial cell size and shape, our population showed a high degree of polymegethism and pleomorphism (MCV of 42.04% and PHC 42.3%). This findings correlate with the fact that in most populations studied, pleomorphism and polymegethism tend to increase as patients age, [35–38] and suggests that elderly Hispanic patients could have more pleomorphism and polymegethism than other ethnicities [1, 7–14].. Surprisingly, the group of ≥ 85 years showed the lowest rate of polymegethism and pleomorphism (33% and 45%, respectively).

Regarding CCT 537 (95% CI 528 to 546), we find interesting that these values are similar to those reported in a previous study performed by our group in younger patients (Mean age: 32.54 ± 12.04 years and Mean CCT: 545.69 ± 36.88 μm). The findings reported in both studies support the idea that Mexican population could present a different mean CCT and “normal” CCT could be redefined for clinical purposes in our context. [39]

Albeit some authors have found differences between gender in endothelial cell parameters [7–10], we found those differences in our population to be minimal with no statistical significance, as resumed in table 2.

Although our results come from a small population, we believe this sets the basis for a prospective study with larger sample size and higher statistical power, which may be eased as specular microscopy becomes more available for the Mexican population.

In conclusion, the endothelial cell characteristics of elderly Mexican Northeastern patients differ from their counterparts from central and south Mexico and other nations. A high prevalence of polymegethism, pleomorphism, and guttata are present, but not in the > 85 year group, where within the sample size studied, the lowest rate of these characteristics was described.

## Declarations

# Ethics approval and consent to participate

All patients enrolled for the study participated voluntarily in the study after reading and signing an informed consent previously reviewed and approved by the Ethics and Research Committees (#ARCC/ECH2019) of our institution following the tenets of the Declaration of Helsinki.

# Consent for publication

Not applicable.

# Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

# Competing interests

The authors declare that they have no competing interests

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# Authors' contributions

JEVG: Concept and design, data analysis/interpretation, critical revision of manuscript, supervision, final approval.

GOM: Data acquisition, data analysis/interpretation, drafting manuscript, final approval.

NMM: Data acquisition, data analysis/interpretation, drafting manuscript, final approval.

JLDH: Data acquisition, data analysis/interpretation, drafting manuscript, final approval.

JHC: Concept and design, data analysis/interpretation, critical revision of manuscript, supervision, final approval.

DLG: Concept and design, data analysis/interpretation, critical revision of manuscript, supervision, final approval.

JZ: Concept and design, data analysis/interpretation, critical revision of manuscript, supervision, final approval.

ARG: Concept and design, data analysis/interpretation, critical revision of manuscript, supervision, final approval.

All authors read and authorized the final version of the manuscript.

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# References

1. Galgauskas S, Norvydaitė D, Krasauskaitė D, Stech S & Ašoklis RS. Age-related changes in corneal thickness and endothelial characteristics. *Clinical interventions in aging.* 2013;8, 1445.
2. Duman R, Çevik MT, Çevik SG, Duman R & Perente I. Corneal endothelial cell density in healthy Caucasian population. *Saudi Journal of Ophthalmology*. 2016; 30(4), 236-239.
3. Qazi Y, Wong G, Monson B, Stringham J & Ambati BK. Corneal transparency: genesis, maintenance and dysfunction. *Brain research bulletin*. 2010;81(2-3), 198-210.
4. Dutt S, Steinert RF, Raizman MB & Puliafito CA. One-year results of excimer laser photorefractive keratectomy for low to moderate myopia. *Archives of Ophthalmology.* 1994;112(11), 1427-1436.
5. Krachmer JH, Mannis MJ, Holland EJ (Eds.), *Cornea*, Elsevier Mosby, New York, 2005.
6. Bourne WM, Nelson LR & Hodge DO. Central corneal endothelial cell changes over a ten-year period. *Investigative ophthalmology & visual science*. 1997; 38(3), 779-782.
7. 7.Padilla MDB, Sibayan SAB & Gonzales CS. Corneal endothelial cell density and morphology in normal Filipino eyes. *Cornea*. 2004; 23(2), 129-135.
8. Snellingen T, Rao GN, Shrestha JK, et al. Quantitative and morphological characteristics of the human corneal endothelium in relation to age, gender, and ethnicity in cataract populations of South Asia. *Cornea*. 2001;20:55–58.
9. Matsuda M, Yee RW, Edelhauser HF. Comparison of the corneal endothelium in an American and a Japanese population. *Arch Ophthalmol.* 1985;103:68–70.
10. Rao SK, Sen PR, Fogla R, et al. Corneal endothelial cell density and morphology in normal Indian eyes. *Cornea*. 2000;19:820–823.
11. Goktas A, Gumus K, Mirza GE, Crockett C, Karakucuk S & Cavanagh HD. Corneal endothelial characteristics in central corneal thickness in a population of Turkish cataract patients. *Eye & contact lens.* 2012; 38(3), 142-145.
12. 1 Hashemian MN, Moghimi S, Fard MA, Fallah MR & Mansouri MR. Corneal endothelial cell density and morphology in normal Iranian eyes. *BMC ophthalmology.* 2006;6(1), 9.
13. Graue-Weichers E, Valdez-Garcıa J, Ramırez-Luquın T & Claros A. Densidad celular endotelial. Estudio en población general de la Ciudad de México. *Rev Mex Oftalmol.* 1989; 63(3), 91-95.
14. Molina DF & Gómez A. Evaluación por décadas de edad del comportamiento de las células endoteliales corneales en población mexicana. *Rev Mex Oftalmol*. 2005;79(2), 93-100.

15. 15.Wallace DK, Melia M. Post hoc Power Calculations. Ophthalmology. 2008; 115(11):2098.
16. 16.Gilbert GE, Prion S. Making Sense of Methods and Measurement: The Danger of the Retrospective Power Analysis. Clinical Simulation In Nursing. 2016;12(8):303-304.
17. 17.Zhang Y, Hedo R, Rivera A, Rull R, Richardson S, Tu XM. Post hoc power analysis: is it an informative and meaningful analysis? General Psychiatry. 2019;32(4):e100069.
18. Kenyon KR, Ghinelli E, Chaves HV. Morphology and pathologic response in corneal and conjunctival disease. In: Foster CS, Azar D, Dohlman CH, eds. Smolin and Thoft's The Cornea: Scientific Foundations and Clinical Practice. 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2005:103-140.
19. Adamis AP, Filatov V, Tripathi BJ, Tripathi RC. Fuchs' endothelial dystrophy of the cornea. Surv Ophthalmol. 1993;38(2):149-168.
20. Yüksel N, Emre E & Pirhan D. Evaluation of corneal microstructure in pseudoexfoliation syndrome and glaucoma: in vivo scanning laser confocal microscopic study. Current eye research. 2016;41(1), 34-40.
21. Geroski DH, Matsuda M, Yee RW, Edelhauser HF. Pump function of the human corneal endothelium. Effects of age and corneal guttata. *Ophthalmology* 1985;92:759-763.
22. Bahn CF, Glassman RM, MacCallum DK, et al. Postnatal development of corneal endothelium. *Invest Ophthalmol Vis Sci*. 1986;4427(1):44
23. Laule A, Cable MK, Hovman CE & Hanna C. Endothelial cell population changes of human cornea during life. *Arch Ophthalmol* 1978;96:2031–5.
24. Ayala G, Díaz ME & Martínez Costa L. Granulometric moments and corneal endothelium status. *Pattern Recognition*. 2001;34, 1219-1227.
25. Joyce NC, Harris DL, Mello DM. Mechanisms of mitotic inhibition in corneal endothelium: contact inhibition and TGF-beta2. I*nvest Ophthalmol Vis Sci.*2002;43, 7:2152–2159.
26. Smith JR & Periera-Smith OM. Replicative senescence: implications for in vitro aging and tumor suppression. *Science* 1996;273:63–7.
27. Norsgaard H, Clark BFC, Rattan SIS. Distinction between diferentiation and senescence and the absence of increased apoptosis in human keratinocytes undergoing cellular ageing in vitro. *Exp Gerontol* 1996;31:655–68.
28. Blake DA, Yu H, Young DL, Caldwell DR. Matrix stimulates the proliferation of human corneal endothelial cells in culture. *Invest Ophthalmol Vis Sci* 1997;38:1119–29.
29. Hoppenreijs VPT, Pels E, Vrensen GFJM, TreVers WF. Effects of platelet derived growth factor on endothelial wound healing of human corneas. *Invest Ophthalmol Vis Sci* 1994;35:150–61.
30. Faragher RGA, Mulholland B, Tuft SJ, Sandeman S, Khaw SPT. Aging and the cornea. *British Journal of Ophthalmology* 1997;81:814–817
31. Laing RA, Sandstrom MM, Berrospi AR, Leibowitz HM. Changes in the corneal endothelial cell function as a function of age. *Exp Eye Res* 1976;22: 587–94.

32. Hoffer KJ & Kraff MC. Normal endothelial cell count range. *Ophthalmology* 1980;87:861–6.
33. Valdez-García J, Pauli KA, Madrid-Valero G, Graue-Wiechers E. Análisis morfométrico automatizado del ojo contralateral en queratopatía bulosa pseudofáquica. *Rev Mex Oftalmol*. 2000; 74(6): 267-270.
34. Valdez-García J, Lozano-Ramírez J, Zavala J. Adult white New Zealand rabbit as suitable model for corneal endothelial engineering. *BMC Research Notes*. 2015; 8:28.
35. Sawa M, Tanishima T. The morphometry of the human corneal endothelium and follow-up of postoperative changes. *Jpn J Ophthalmol* 1979; 23:337–350.
36. Suda T. Mosaic pattern changes in human corneal endothelium with age. *Jpn J Ophthalmol*. 1984;23:331–338.
37. Yee RW, Matsuda M, Schultz RO, et al. Changes in the normal corneal endothelial cellular pattern as a function of age. *Curr Eye Res* 1985;4: 671– 678.
38. 38.Carlson KH, Bourne WM, McLaren JW, et al. Variations in human corneal endothelial cell morphology and permeability to fluorescein with age. *Exp Eye Res* 1988;47:27–41
39. Valdez-García J, Hernandez-Camarena J, Lozano-Ramírez J, Zavala J, Loya-García D, & Merayo-Lloves J. Correlation of age, corneal curvature and spherical equivalent with central corneal thickness. Revista Mexicana de Oftalmología, 2017; 91(4), 172-176.

# Tables

***Table 1.*** *Endothelial cell density and morphology according to age.*

| Age Group(y) | No. Of eyes | Mean Age (y) | MCD (cells/mm2) | MCA (µm2) | MCV (%) | Hexagonality(%) | MCCT (µm) | Mean No. of cells studied |
|---|---|---|---|---|---|---|---|---|
| 65-69 | 23 | 66.7±1.6 | 2458.0±484.0 | 433.7±146.1 | 42.1±9.8 | 41.8±7.5 | 525.0±28.6 | 233.6 |
| 70-74 | 23 | 71.4±1.5 | 2177.0±659.2 | 515.5±210.9 | 42.9±9.0 | 42.8±9.7 | 535.7±37.4 | 180 |
| 75-79 | 13 | 77.61+1.3 | 2126.7±593.7 | 520.0±198.1 | 40.4±5.3 | 41.1±6.0 | 548.4±39.9 | 197.2 |
| 80-84 | 7 | 82.4±1.0 | 2026.8±869.7 | 601.6±298.4 | 48.7±19.5 | 38.3±14.6 | 547.8±61.3 | 177.5 |
| 85-90 | 9 | 86.1±1.4 | 2404.0±360.8 | 423.9±59.9 | 36.9±7.4 | 46.5±7.5 | 545.1±37.1 | 228.4 |

***MCD:*** *mean endothelial cell density,* ***MCA:*** *mean cell area,* ***MCV:*** *mean coefficient of variation,* ***MCCT:*** *mean central corneal thickness.*

***Table 2.*** *Endothelial Cell Parameters and Central Corneal Thickness by Gender.*

| Measurement parameter | Female | Male | P value |
|---|---|---|---|
| **Mean age (yr)** | 76.08±7.16 | 71.71±5.87 | 0.01 |
| **MCD (cells/mm$^2$)** | 2167.38±615.04 | 2365.42±570.13 | 0.15 |
| **MCA (μm$^2$)** | 514.86±200.03 | 462.37±181.28 | 0.24 |
| **MCV (%)** | 43.57±10.54 | 40.55±9.55 | 0.20 |
| **Hexagonality (%)** | 40.68±9.29 | 43.79±8.23 | 0.13 |
| **MCCT (μm)** | 535.24±41.27 | 538.53±35.43 | 0.71 |

***MCD:*** *mean endothelial cell density,* ***MCA:*** *mean cell area,* ***MCV:*** *mean coefficient of variation,* ***MCCT:*** *mean central corneal thickness.*

***Table 3.*** *The average endothelial cell density (cells/mm$^2$) of healthy eyes among different population.*

| Population | First author | Average endothelial cell density (cells/mm$^2$) | Age (years) | Number of eyes examined |
|---|---|---|---|---|
| Lithuania | Galgauskas[1] | 2,366 | 60 – 89 | 158 |
| Philippines | Padilla[7] | 2780.45 | 61 – 86 | 200 |
| India | Rao[10] | 2404 | 60 – 87 | 142 |
| Turkey | Goktas[11] | 2,215 | 61 – 90 | 371 |
| Iran | Hashemian[12] | 1681.61 | 61 – 85 | 225 |
| Central Mexico | Graue[13] | 1805.33 | 60-89 | 25 |
| Central Mexico | Molina[14] | 1910 | 60 – 89 | 50 |
| North Mexico | Valdez et al. | 2268 | 65-90 | 75 |

# Figures

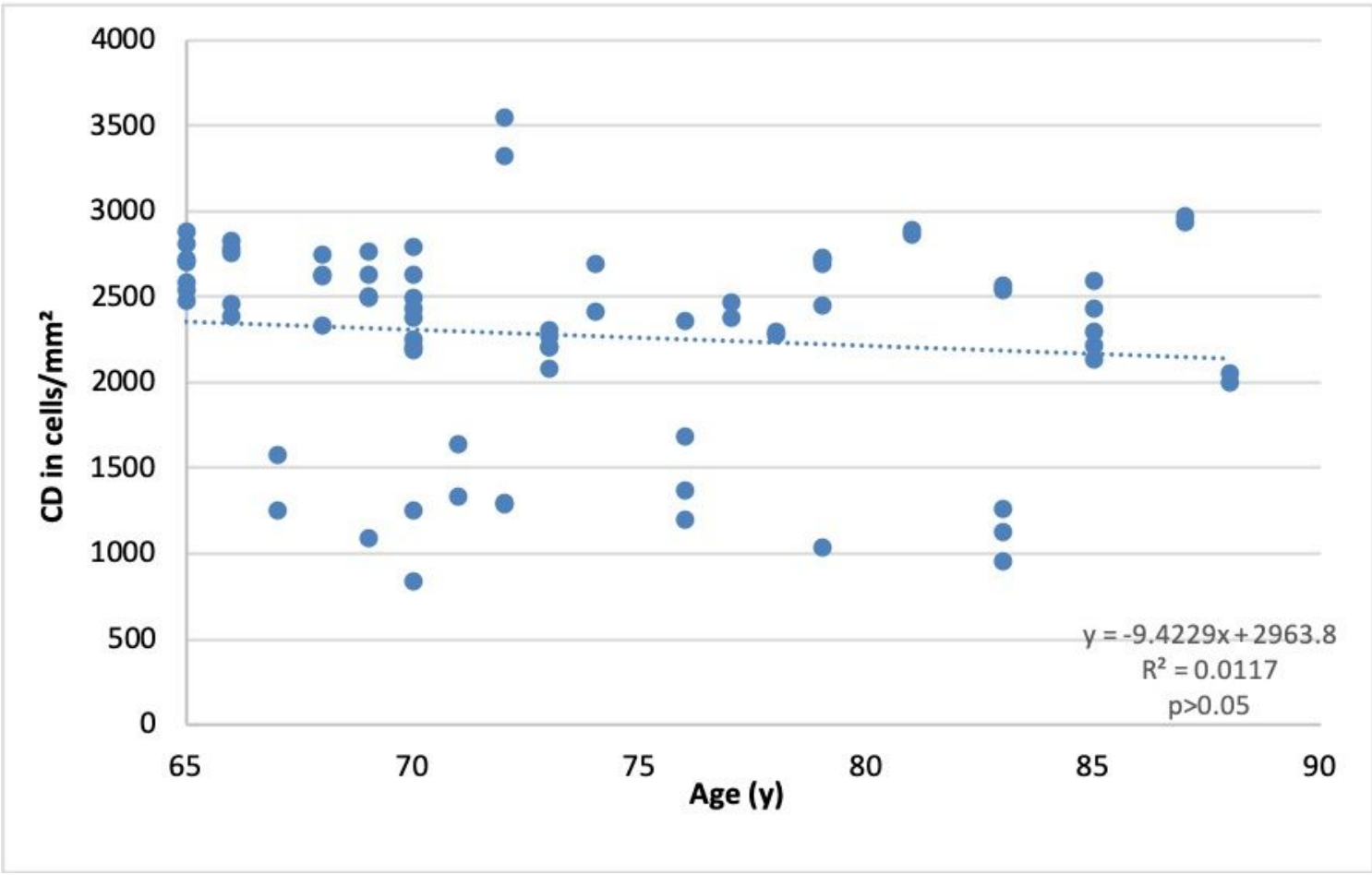
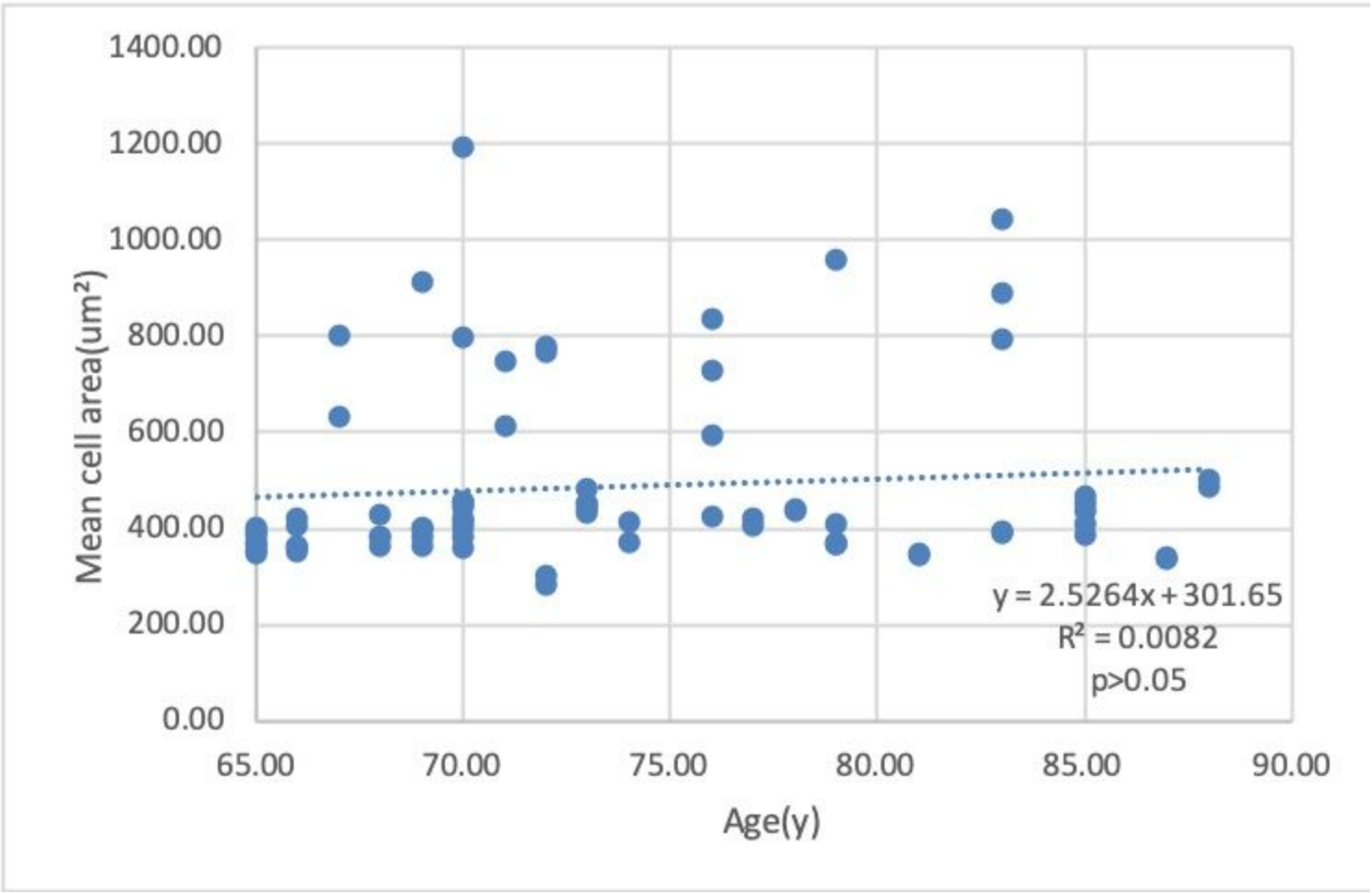



**Figure 1**

Changes in mean cell density among age groups




## Figure 2

Mean cell area among age groups.

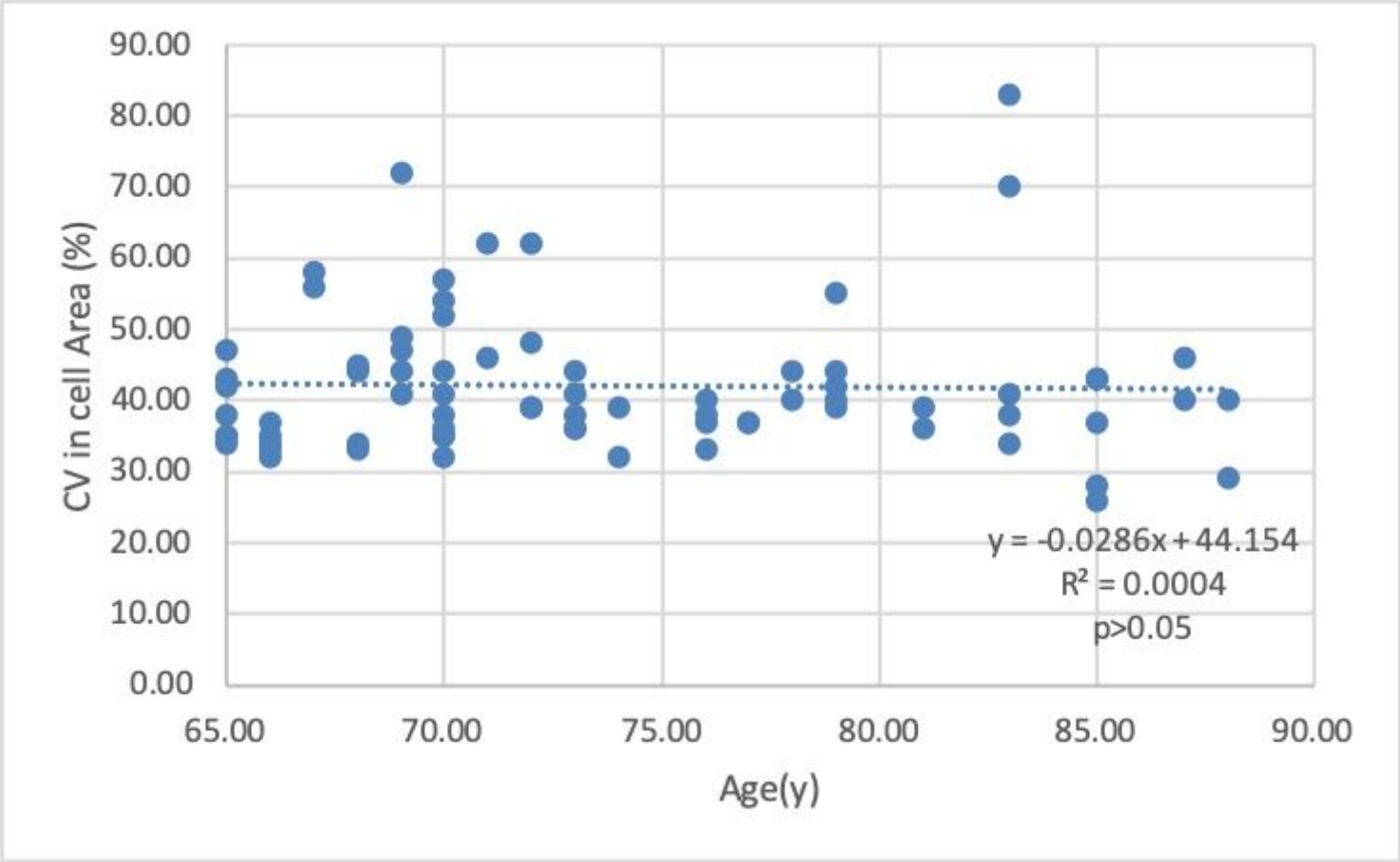



**Figure 3**

Mean coefficient of variation for all age groups.

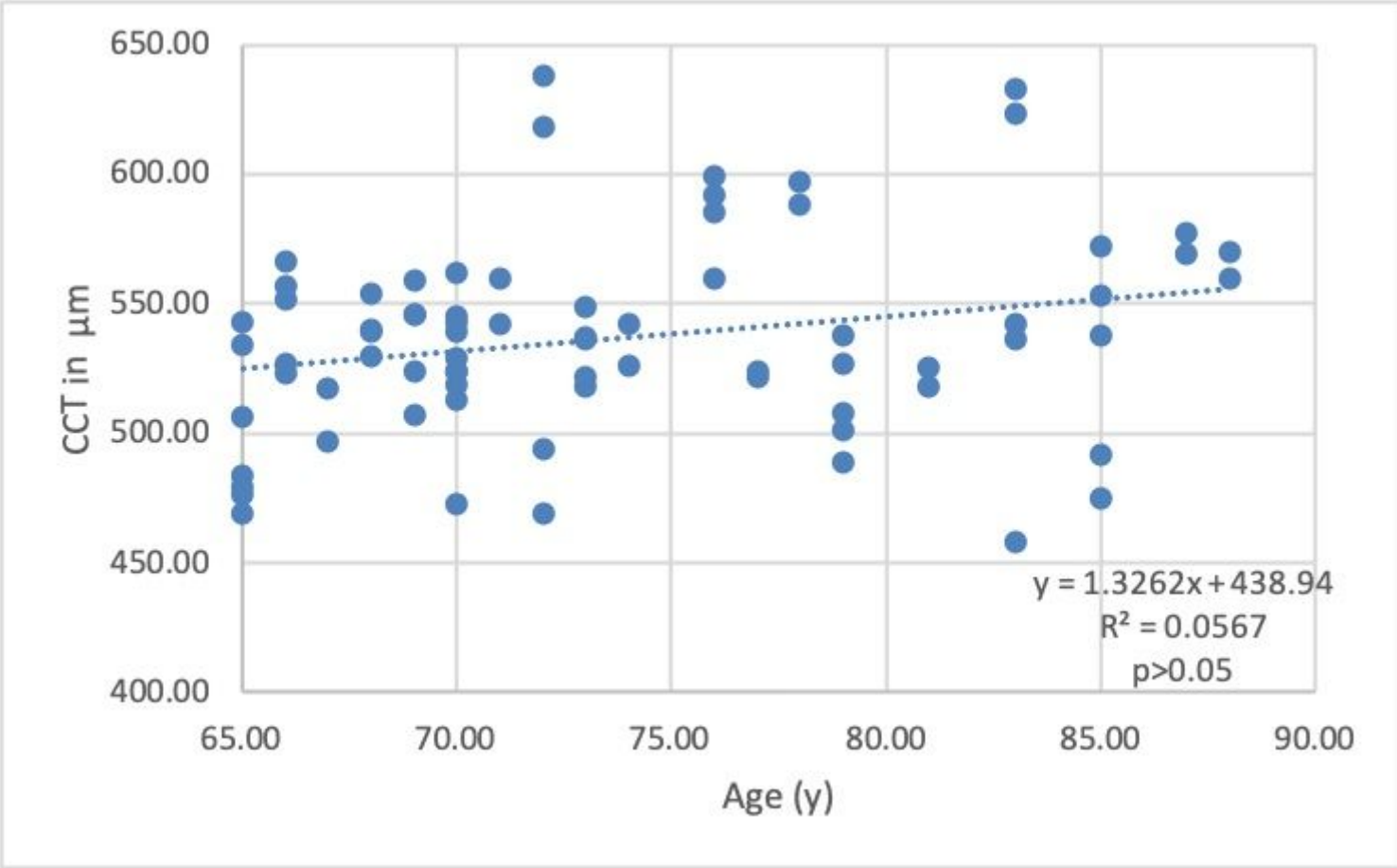



**Figure 4**

Mean central corneal thickness for all age groups.