CORRELATION OF AGE WITH CENTRAL CORNEAL THICKNESS AND CORNEAL ENDOTHELIAL CELL DENSITY IN PAKISTANI POPULATION

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ABSTRACT

Objective: Correlation of age with central corneal thickness (CCT) and corneal endothelial cell density (ECD) in Pakistani population.

Study Design: Descriptive cross sectional study.

Place and Duration of Study: Armed Forces Institute of Ophthalmology Rawalpindi from Apr 2016 to Oct 2016.

Material and Methods: CCT and ECD was measured in 330 eyes of 165 patients, aged between 21-70 years of age. Patients were further divided into five age groups. Three readings were taken for each eye, and mean of three readings was used for the analysis. Pearson correlation was calculated between CCT, ECD and age.

Results: A total of 330 eyes of 165 patients were studied. Out of study population, 81 (49.09%) were males and 84 (50.90%) were females. Mean ECD (cell/mm^2) was 3063.85 ± 234.65 cells/mm^2 and 256.42 ± 475.06 cells/mm^2 in patients aged 21–30 years, and 61–70 years respectively. Mean CCT (µm) was 544 ± 18 µm and 528 ±21 µm in patients aged 21–30 years, and 61–70 years respectively. A statistically significant inverse correlation was observed between age and corneal ECD (r=−0.718, p<0.01) and age and CCT (r=−0.230, p<0.01).

Conclusion: Both CCT and corneal ECD decrease significantly with age in Pakistani population, with statistically more decrease in ECD with age, than CCT.

Keywords: Age-related changes, Central corneal thickness, Endothelial cell density.

INTRODUCTION

Cornea, the optical and protective outermost layer of the eye, is a transparent structure with multifaceted roles for normal physiological and anatomical function. It is a multilayered structure, with each layer performing specific physiological tasks for necessary functioning of human eye. Each layer of the cornea has separate embryological origin, function, integrity and regeneration potential. Globally, pathologies related to cornea are the 4th leading cause of blindness. In Pakistan, corneal blindness is slightly more prevalent owing to lack of transplant services and awareness[1]. The measurement of average central corneal thickness (CCT) is variable due to difference in measuring instruments, age, race, gender and other important factors[2]. CCT measures central part of the cornea only, as normal human cornea gets slightly thickened towards the limbus. Since the measurement of CCT is variable due to variety of factors, its correct estimation is of paramount importance for measuring reliable intraocular pressure (IOP) level[3]. It has been learnt by different studies that thin corneas are important risk factors for development of different types of glaucoma[4]. It is important to measure CCT in order to diagnose glaucoma, monitor response to treatment of corneal edema, evaluation of patients for different refractive surgical procedures and diagnosis of hereditary diseases related to cornea. The innermost layer adjacent to anterior chamber is endothelium. It has a peculiar feature, that it is incapable of regeneration. This makes it most significant, as diseases and degenerations preferentially affecting this layer result in permanent loss of corneal clarity. Main function of this layer is to maintain a dehydrated state of the cornea, which is mandatory for optimal optical performance and clarity. The endothelium is studied using specular

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microscopy, which non-invasively studies characteristics of corneal endothelium, ECD, structure and hexagonality. Different studies in different ethnic groups have revealed different rate of loss of corneal ECD with age, ranging from 0.3-1.1% per year[5]. Endothelial damage and decrease in ECD can be due to congenital corneal dystrophies, as well as due to acquired clinical conditions like chronic intraocular infections and inflammations, iatrogenic damage during cataract surgery, glaucoma, retained nuclear fragments after surgery and keratoconus[6]. Age is an important parameter which leads to anatomical, physiological, structural and functional changes in human eye, as well as cornea. Different studies have revealed change in CCT and corneal ECD of different levels with advancing age[7]. There occurs quite significant variation in literature about the rate of CCT and ECD change in human cornea with age, depending upon gender, race and measurement techniques[8]. Limited local data are available regarding the effect of age on CCT and ECD, while international data shows variability of these counts in different populations. The objective of study was to evaluate correlation of age with CCT and ECD in Pakistani population.

PATIENTS AND METHODS

This was a descriptive cross sectional study, carried out in Armed Forces Institute of Ophthalmology (AFIO) Rawalpindi Pakistan, from April 2016 to October 2016, after taking written informed consent from patients and approval from institute ethical review committee. A total of 330 eyes of 165 patients were analyzed. Sample size was calculated using World Health Organization (WHO) sample size calculator, keeping confidence interval at 95% and level of significance at 5%[9]. Patients between 21-70 years of age, of either gender, with healthy corneas and willing to undergo evaluation were selected through non-probability consecutive sampling. Patients with own or family history of corneal dystrophies, trauma, uveitis, glaucoma, history of corneal ulcer, intraocular surgery, ocular allergies, trachoma, and chemical injury were excluded. Patients were further placed into five

Table-I: Data of study population according to age groups (n=165).

Age Group (years)	Number of Eyes	ECD (Cells/mm²)		CCT (µm)	
		Mean	SD	Mean	SD
21-30	66	3063.85	234.65	513.03	32.78
31-40	66	2962.02	133.37	503.68	31.26
41-50	66	2732.22	180.81	494.18	31.76
51-60	66	2476.77	278.31	501.75	33.11
61-70	66	2256.42	475.06	490.59	30.64
p-value* (Age group and CED/CCT)		<0.001		0.001	

*One way ANOVA test

Table-II: Data of study population according to gender (n=165).

Gender	Number of Eyes	ECD (Cells/mm²)		CCT (µm)	
		Mean	SD	Mean	SD
Male	162	2708.46	420.89	501.12	32.25
Females	168	2688.414	406.6888	500.20	33.19
p-value* (Gender and CED/CCT)		0.660		0.799	

*Independent t-test

Table-III: Pearson's correlations between age and CCT, ECD (n=165).

	Between Age and ECD	Between Age and CCT
Pearson's Correlation	- 0.718	- 0.230
Significance (2-tailed)	<0.001	<0.001

age groups. Each group included 66 eyes and a 10-year interval: 21-30 years, 31-40 years, 41-50 years, 51-60 years and 61-70 years. Detailed history was taken, and all patients underwent detailed anterior segment and posterior segment examination by single researcher to exclude bias. CCT and ECD measurements were taken using non-contact, Topcon SP 3000P specular microscope. Three readings were taken for each eye, and central 100 cells were analyzed only for endothelial evaluation, excluding abnormal cells. Mean of three reading was eventually used for data analysis. Data was collected and analyzed in the statistical package for social science (SPSS) version 20.0. Mean and standard deviation (SD) were calculated for continuous variables (CCT, ECD). Categorical variables (gender) were presented by frequency and percentages. Pearson correlation (r) was calculated between CCT, ECD and age. Relation of age groups and gender with CCT and ECD was analyzed using one way ANOVA test and Independent t-test respectively. A *p*-value of ≤0.05 was taken as statistically significant.

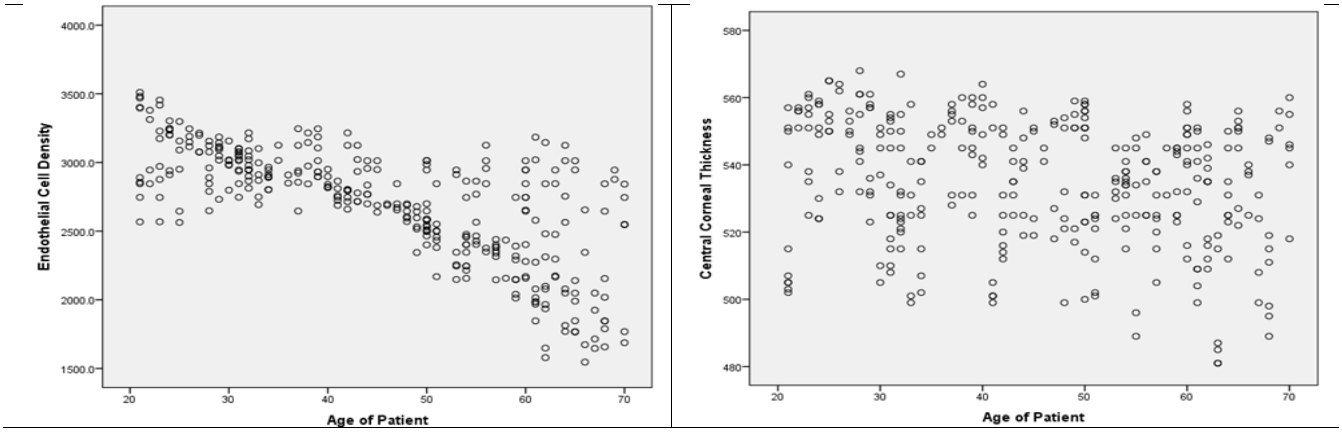

Figure: Graphical distribution of CCT and ECD with regards to age (n=165).

RESULTS

A total of 330 eyes of 165 patients were studied. Out of study population, 81 (49.1%) were males while 84 (50.9%) were females. Mean age of study population was 45.37 ± 14.52 years. Mean CCT of study population was 500.65 ± 32.69 µm, while mean ECD of study population was 2698.25 ± 413.21 cells/mm^2. Mean CCT and ECD of each age group is given in table-I. Difference of mean CCT and mean ECD between age groups was statistically significant (p≤0.005). Mean CCT and ECD with regards to gender is given in table-II. Difference of mean CCT and mean ECD between both genders was not statistically significant (p=0.799 and 0.660 respectively). Pearson correlation of age with CCT and ECD is given in table-III. Both CCT and ECD have inverse and statistically significant correlation with age. Graphical distribution of CCT and ECD with regards to age is given in figure.

DISCUSSION

Analysis of CCT and ECD measurement is of highly clinical significance in ophthalmic practice. Both measurements have importantrole in management of different corneal pathologies, watching response to treatment and planning future therapeutic goals. In our study, we included people from age ranging from 21-70 years. This was to include sufficient number of people from all age groups to estimate the characteristics of corneal endothelium. We used non-contact specular microscope for measurement of CCT and ECD. Though, it allows corneal parameters measurement with ease, CCT measured appears to be unreliable owing to tear film and air interface irregularities. However, the results were consistent with data from most of the studies. We found that with advancing age, ECD changes

significantly. The pearson correlation was statistically significant between age and ECD, and a strong negative correlation was observed. This is consistent with literature and latest studies done on the subject[10] Though, we did not find a significant difference between different age groups and ECD. The reason may be attributed to age groups distribution and large age group made (10 years). We did not evaluate the frequency of decrease in ECD with every year. In a study conducted in Portugal, it was observed that annual rate of decrease in ECD was 5-6%[11]. Variable rates of decrease in ECD were observed, amounting to as high as 1% every year[12]. Our results are consistent with findings of other studies, with little variation[9,13]. The ECD thus shows significant decrease with age, in Pakistani population, and results of this study are in coherence with research available in literature. The cause of decrease in ECD is not known exactly. Since the decaying cells cannot regenerate, the cells enlarge to take their place and lead to change in structure of corneal endothelium. Different theories have tried to explain the endothelial loss, the most striking being role of energy induced oxidative stress and damage leading to apoptosis or necrosis[14]. Literature search revealed that ECD shows rapid and aggressive decrease from 12 weeks till 40 weeks of gestation[15]. We also found that age groups showed statistically significant difference in CCT in study population. This was also verified, when pearson correlation between age and CCT showed statistically significant correlation. Our findings are more reliable as we used non-contact method to evaluate CCT, thus not altering shape and structure of cornea. Our findings are different from inferences drawn by Prasad *et al*, who did not find any statistically significant correlation between age and CCT[16]. This study was conducted on eye undergoing laser refractive procedures, and are ought to have abnormal CCT and ECD than normal population. Since, we did not include eyes with refractive errors in our study, our results are more reliable than mentioned study. Another study found no correlation of age with CCT[17]. The mentioned study was conducted on Japanese population, who have a significant number of ametrope patients in their population. However, few studies have found consistent results seen by our research. One study showed that CCT displayed a slight but non-significant inverse correlation with age, as seen by our study[18]. Similar results were seen by Niederer *et al*, where statistically significant decrease in CCT was seen with advancing age[19].

LIMITATIONS OF STUDY

The study has few limitations. The patients included were aged between 20-70 years. Inclusion of children will reveal better analysis of ECD and CCT changes, as the decrease is suggested to be aggressive in early ages of life. Assessment of CCT with other non-contact techniques like scheimpflug pachymetry and ultrasonic pachymetry will result in more reliable assessment of CCT. Most importantly, we included only emmetropic patients in the study. Inclusion of patients with variety of refractive errors will reveal more reliable assessment of ECD and CCT in Pakistani population.

CONCLUSION

Both CCT and corneal ECD decrease significantly with age in pakistani population, with statistically more decrease in ECD with age, than CCT. The study also provides relevant normative data of Pakistani population, which can be used as reference in future studies and research.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

REFERENCES

1. Siddiqui R, Chaudhry T, Lakhundi S, Ahmad K, Khan NA. Failure of chemotherapy in the first reported cases of Acanthamoeba keratitis in Pakistan. Pathog Glob Health 2014; 108: 49-52.
2. Sadoughi MM, Einollahi B, Einollahi N, Rezaei J, Roshandel D, Feizi S. Measurement of Central Corneal Thickness Using Ultrasound Pachymetry and Orbscan II in Normal Eyes. J Ophthalmic Vis Res 2015; 10: 4-9.
3. Keel S, Malesic L, Chan SP. Diurnal variation in central corneal thickness and intraocular pressure in eyes with

pseudoexfoliation syndrome without glaucoma. Indian J Ophthalmol 2014; 62: 1072-76.
4. Zar G, Voigt M, Al-Arabi Z, Lachkar Y. Primary open-angle glaucoma (POAG), retinal vein occlusions (RVO) and central corneal thickness (CCT): what is the relationship. J Fr Ophtalmol 2013; 36: 449-54.
5. Zavala J, López Jaime GR, Rodríguez Barrientos CA, Valdez-Garcia J. Corneal endothelium: developmental strategies for regeneration. Eye (Lond) 2013; 27: 579-88.
6. McLaren JW, Bachman LA, Kane KM, Patel SV. Objective assessment of the corneal endothelium in Fuchs' endothelial dystrophy. Invest Ophthalmol Vis Sci 2014; 55: 1184-90.
7. Gipson IK. Age-related changes and diseases of the ocular surface and cornea. Invest Ophthalmol Vis Sci 2013; 54: ORSF 48-53.
8. Beuschel R, Hofmann T, Messerli J. Is the decrease in corneal endothelial cell density in relation to age linear?. Klin Monbl Augenheilkd 2015; 232: 375-79.
9. Galgauskas S, Norvydaitė D, Krasauskaitė D, Stech S, Ašoklis RS. Age-related changes in corneal thickness and endothelial characteristics. Clin Interv Aging 2013; 8: 1445-50.
10. Niederer RL, Perumal D, Sherwin T, McGhee CN. Age-related differences in the normal human cornea: a laser scanning in vivo confocal microscopy study. Br J Ophthalmol 2007; 91: 1165–69.
11. Jorge J, Queiros A, Peixoto-de-Matos SC, Ferrer-Blasco T, Gonzalez-Meijome JM. Age-related changes of corneal endothelium in normal eyes with a non-contact specular microscope. J Emmetropia 2010; 1: 132-39.
12. Cheng H, Jacobs PM, McPherson K, Noble MJ. Precision of cell density estimates and endothelial cell loss with age. Arch Ophthalmol 1985; 103: 1478-81.
13. Ashraf KM., Saeed M.U, Zia R. Corneal endothelial cell density in a normal Pakistani population. Eye 2006; 20: 116-18.
14. Abib FC, Barreto Junior J. Behavior of corneal endothelial density over a lifetime. J Cataract Refract Surg 2001; 27: 1574-78.
15. Ko MK, Park WK, Lee JH, Chi JG. A histomorphometric study of corneal endothelial cells in normal human fetuses. Exp Eye Res 2001; 72: 403-09.
16. Prasad A, Fry K, Hersh PS. Relationship of age and refraction to central corneal thickness. Cornea 2011; 30: 553-55.
17. Kamiya K, Shimizu K, Ohmoto F. Effect of aging on corneal biomechanical parameters using the ocular response analyzer. J Refract Surg 2009; 25: 888-93.
18. Jorge J, Queiros A, Peixoto-de-Matos SC, Ferrer-Blasco T, Gonzalez-Meijome JM. Age-related changes of corneal endothelium in normal eyes with a non-contact specular microscope. J Emmetropia 2010; 1: 132-39.
19. Niederer RL, Perumal D, Sherwin T, McGhee CN. Age-related differences in the normal human cornea: a laser scanning in vivo confocal microscopy study. Br J Ophthalmol 2007; 91: 1165-69.

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