Relationship of Corneal Endothelial Morphology and Central Corneal Thickness to Age and Sex in Normal Healthy individuals in our Community

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Abstract

Background: Central corneal thickness and corneal endothelial morphology was studied along it's relationship with age and sex.

Objective: To determine the normative data of central corneal thickness and endothelial morphology in our population.

Methodology: This is a Cross sectional study. The study was done at Ophthalmology Department, FRPMC in accordance with the declaration of Heliniski from March 2021 to August 2021 with approval from Institutional review board. All healthy individuals aged 20 to 70 years presenting with any ocular complain but no corneal pathology were included. Individuals with any systemic and ocular co morbidity were excluded. After complete ocular examination corneal specular microscopy was done using REXAM SPM-700 corneal specular microscope. In our study we analysed CCT, ECD, MCA, CV and hexagonality. The data was collected and recorded on Excel spreadsheet and then transformed to SPSS version 22 for statistical analysis.

Results: 724 eyes from 362 individuals were studied for CCT and endothelial morphology using Rexam SPM-700 microscope. There were 241(66.6%) males and 121(33.4%) females with mean age 38.33±10.17 years. Among 724 eyes we found CCT (508.43±33.4um), ECD (2565.12±254.15cell/mm^2), AVG (393.81±40.72um^2), CV (39.54±6.43%) and Hexa (46.18±6.64%). Statistically there was no significant difference among right and left eyes of study population as well as gender wise. There is statistically significant inverse correlation of ECD with age ($p<0.00$, r:-0.19). However, statistically insignificant inverse correlation is found for CV and Hexa with age ($p<0.17$, r:-0.05) ($p<0.70$, r:-0.014) respectively.

Conclusion: Our study reports the normative corneal endothelial morphology and thickness in Pakistani population attending FRPMC Ophthalmology Department. We also found that Central corneal thickness and Endothelial cell density decreases with aging and no statistical difference gender wise.

Key Words: Central Corneal Thickness, Endothelial Cell Morphology, Age, Sex

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Introduction

The cornea along with air tear interface contributes to two thirds of the refractive power of the eye. Besides providing structural integrity to eyeball it also protects from invasion of micro-organisms. Being prolate it is steeper in center and flatter towards the periphery. The average central thickness is 550 um and 650 um in periphery. It is an avascular, transparent tissue, consists of five layers each of which has unique and important role in keeping the cornea transparent.

The endothelium is the inner most part of cornea, monolayered, hexagonal derived from neural crest cells. The endothelium has tight junctions with adjacent cells which possess NaK ATPase pump[1], these plays a pivotal role in maintaining deturgescent state of corneal stroma (78% water). This ability to hydrate the cornea is affected by functional reserve of the endothelial cells[2]. The endothelial cells are devoid of regeneration capacity hence mature endothelial cells replace any loss/injured cells by expansion and migration to that area. Loss of one hexagonal cell among 100 endothelial cells causes 1% increase in mean cell area but 6% decrease in hexagonal cell population[3]. There is continuous and progressive change in the endothelial cell morphology through one's life. The number of endothelial cells at birth is 5000 to 6000 cells/mm^2 reducing to approx. 2600 cells/mm2 at eighth decade of life[1,4]

The endothelial cell count, size and shape all relate to level of deturgescence of corneal stroma. Thus corneas with less than 500-700/mm^2 endothelial cells are at risk of developing edema following intraocular surgeries. Nayak[5] found 7.4% loss of endothelial cell density following routine phacoemulsification. Yeniad[6] study reveals 10.8% loss of ECD following phacoemulsification for senile cataract. Reported average annual rate of endothelial cell loss among normal corneas is 0.3%-0.5%[7]. A healthy cornea has atleast 60%[5] of hexagonal endothelial cells, which declines with increasing age from 75% to 60%. The

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coefficient of variation is the most sensitive index of corneal endothelial dysfunction and has normal value of 30%[8]. Any stress to the corneal endothelium may cause variation in cell size, shape and count. Examples of such stress include hypoxia, hyperglycemia, surgical or nonsurgical trauma, drug toxicity (intracameral fluid flow or drugs), and glaucoma. Thus diabetic patients have decreased endothelial cell count as compared to their age matched controls[8] and have thicker corneas[9].

Specular microscopy is a simple, noninvasive tool that images the corneal endothelium to assess its morphology analyzing size, shape density and distribution. It's being used in clinical setting to assess the health of the cornea and in particular the eye banks to assess endothelial morphology to provide quality donor corneas. Knowledge of ECD gives an estimated risk of postoperative corneal decompensation in patients planned for surgical procedures, for instance phakic intraocular lens implantation, phacoemulsification. There is continuous change in endothelial cell morphology with increasing age but significant variation do exist among races and ethnic groups[1], therefore normative data is required to determine the health of corneal endothelium for a particular race/population.

Methodology

This Cross sectional study was done at Ophthalmology Department, Fazaia Ruth Pfau Medical College (FRPMC) in accordance with the declaration of Heliniski from March 2021 to August 2021 with approval from Ethics Review Committee, letter no. IRB/05 dated 1-03-2021. The sample size calculated using Taro Yamane Method with margin of error being 0.05 was 534.

All Individuals in good general health aged 20 years to 70 years with any ocular complain but having no corneal pathology were included in our study.

Our exclusion criteria included presence of any systemic or ocular disease which can adversely affect the endothelial morphology like Diabetes mellitus, previous surgical or nonsurgical ocular trauma, keratoconus, corneal degeneration or dystrophy, intraocular inflammation, dry eyes, contact lens wear.

All the patients initially had visual acuity assessment, refraction and slitlamp examination for anterior segment. Then the corneal specular microscopy was done using REXAM SPM-700 corneal specular microscope. The device auto tracts and auto focuses the cornea, captures 16 images in 2 seconds, the best image is selected automatically for analysis. The parameters assessed by this specular microscope are central corneal thickness (CCT), Number and Density of Endothelial Cell (ECD), Average cell area (AVG), Standard deviation (SD) and Coefficient of Variation (CV) of cell area plus rate of cell hexagonality (6A). The informed consent was obtained from all study participants. The parameters we studied are CCT, ECD, MCA, CV and hexagonality. The data was collected and recorded by the examiner on Excel spreadsheet and then transformed to SPSS version 22 for statistical analysis. Independent t-test was applied to compare different variables for statistical significance. Pearson Correlation defined the relation of different variables with age.

Results

A total of 724 eyes from 362 individuals were studied for CCT and endothelial morphology using Rexam SPM-700 microscope. There were 241(66.6%) males and 121(33.4%) females with mean age 38.33±10.17 years in our study. Among 724 eyes we found CCT (508.43±33.4μm), ECD (2565.12±254.15cell/mm^2), AVG (393.81±40.72μm^2), CV (39.54±6.43%) and Hexa (46.18±6.64%). The studied variables of endothelial morphology for different age groups are shown in Table I.

Table I: Comparison among different age groups

Group (years)	No of eyes (724)	Age (years) Mean± SD	CCT (μm) Mean± SD	ECD (cells/mm2) Mean± SD	AVG (μm2) Mean± SD	CV (%) Mean± SD	A (%) Mean± SD
21-30	174	25.69±3.18	513±35.14	2620.15±221.53	384.30±31.77	40.57± 6.37	46.05± 7.78
31-40	274	36.19±2.75	508.94±33.06	2575.50±254.02	392.32±41.66	39.04±7.24	46.23±6.77
41-50	190	44.28±2.68	508.37±29.41	2543.39±239.52	396.62±37.40	39.61±5.53	46.29±6.48
51-60	62	55.10±2.78	494.18±32.42	2513.45±316.94	404.39±53.35	38.39±5.62	46.23±6.91
61-70	24	64±1.89	502.08±45.92	2353.25±274.69	430.33±49.16	40.29±4.84	45.71±4.86

CCT(Central Corneal Thickness), ECD(Endothelial cell density),AVG(Average cell area), CV(coefficient of variation), A(Hexagonality)

Table-II: Laterality and Gender wise comparison of CCT and endothelial cell morphology

	Right Eye n-362 Mean± SD	Left Eye n-362 Mean± SD	P-Value	Male n=482 Mean± SD	Female n=242 Mean± SD	P-Value
CCT (um)	508.76±33.44	508.10±33.40	0.79	38.22±10.27	38.56±10.01	0.76
ECD (cells/mm2)	2549.99±251.16	2580.26±256.57	0.10	509.39±32.48	506.51±35.15	0.27
AVG (um2)	396.10±40.72	391.52±40.65	0.13	2573.41±243.18	2548.63±274.50	0.21
CV (%)	39.42±6.27	39.67±6.60	0.61	392.16±38.55	397.11±44.625	0.12
A-Hex (%)	46.51±6.54	45.85±6.73	0.18	39.16±6.02	40.30±7.14	**0.02**

CCT(Central Corneal Thickness), ECD(Endothelial cell density),AVG(Average cell area), CV(coefficient of variation), A(Hexagonality)

Table III: Central Corneal Thickness and Endothelial Cell density among different races

	Central corneal Thickness µm			Endothelial Cell Density Cells/mm^2		
	Current Study n (724)	**Indian Pop n (483)**	**Egyptian Pop n (568)**	**Current Study n(724)**	**Indian Pop n (483)**	**Iranian Pop N(422)**
21-30 yr	513±35.14	541.9±27.4	525.92±46.83	2620.15±221.53	2782±250	2407±399
31-40 yr	508.94±33.06	526.9±61.9	518.65±67.99	2575.50±254.02	2634±288	2245±349
41-50 yr	508.37±29.41	540.1±29.4	503.62±28.57	2543.39±239.52	2408±274	2071±340
51-60 yr	494.18±32.42	532.7±27.7	516.92±34.56	2513.45±316.94	2438±309	1939±344
61-70 yr	502.08±45.92	530.4±80.0	512.59±42.71	2353.25±274.69	2431±357	1775±348

Statistically there was no significant difference among right and left eyes of study population as well as among gender. (Table II)

There is statistically significant inverse correlation of ECD with age ($p<0.00$, r:-0.19). However statistically insignificant inverse correlation is found for CV and Hexa with age ($p<0.17$, r:-0.05) ($p<0.70$, r:-0.014) respectively.

Discussion

Various Researchers[11,14,15,17] have studied the relationship of Corneal thickness and endothelial morphology with age, sex, IOP, Diabetes Mellitus, glaucoma both nationally and internationally.

Manual, semi-automatic and automatic strategies can be used to do endothelial cell count. The technique used and software installed in specular microscopes of different manufactures can affect the outcome for endothelial cell morphology.[12] In our study we used non-contact specular microscope which auto tracks the cornea to capture the image. We used the automatic image selected and analyzed by the machine.

To the best of my knowledge as per literature search it is the only study done on Rexxam SPM-700 specular microscope.

We categorized our study population according to their age. In our study the largest participants were in 31-40 years age category while age group 61-70 years has least number of participants, who may not be the true representative for this age range. One explanation to this could be because of corona pandemic, elderly patients avoided unnecessary hospital visits, also patients in this age group have pseudophakia and co morbids like Diabetes, which were excluded. Similarly small sample of 61-70 yrs age group was seen by Ono Takashi.[13]

The number of endothelial cells counted to obtain a max accuracy per image has been suggested by Ling et to atleast 30 cells per image[14] others prefer 75 to 100 cells per image. The average number of endothelial cells used to assess endothelial morphology in current study is 218.64±37.97.

In current study there was no significant difference of studied variables between right and left eyes (Table:II) similar observation was made by other researchers.[15,16] Sturrocket al[17] noted ECD of both eyes in an individual to be constant. We found significant variation in cell size ($p<0.02$) among male versus female (Table:II). Male showed less variation in cell size than female as one ages. Similar difference was noted in Thai population.[18] Qamaret al[15] found no gender based variation in cell size but significantly higher CCT in females. Tayyabet al[19] study shows no difference in CCT among male and female.

The CCT measurements can vary in same individual depending on the type of instrument used. The mean CCT in our study was 508.43±33.4um, which is comparable to seen by Qamar Islam et al and Bilal

Hassan et al.[15,16] Similar CCT was observed in another study done by Tayyabet al.[19] A noncontact specular microscope was used in all these studies. CCT in current study was lower than seen by Roomasaet al,[20] they measured CCT using ultrasonic pachymetry. However, Gasser has found difference in same individual using noncontact specular microscope of different companies.[21] The CCT has steadily declined with increasing age upto sixth decade, however, there is slight increase in seventh decade in our study. The difference in CCT with other nations is evident.

CCT in our study population is low, thus there are increased chances of recording falsely low IOP and missing glaucoma cases.

The mean ECD in our study was 2565.12±254.15, slightly lower than studied by Islam[5] , Bilal[6] and Ashraf [22] however, no of eyes we studied was largest than all these, also the noncontact specular microscope used was of different manufacturer. This can be a possible reason for variation in outcome of our study. In comparison to studies done in our neighboring countries the ECD in our study population is lower than Indian[4] and Thai[18] population but higher than studied Iranian population.[11] In contrast to American and Indian population Iranian[14] population has reduced endothelial cell count and hence may be more at risk of pseudophakic bullous keratopathy and so is ours. Japenese population have highest ECD than other races[23] and thus have minimum risk of postoperative corneal decompensation. No correlation was seen between CCT and ECD (r:0.00, $p<0.22$). Hence CCT cannot be the true representative of endothelial health.

Claesson[24] found 43% incidence of persistent corneal edema following cataract surgery, preexisting endothelial disease and phacoemulsification being important risk factor. Tsaousis[25] study reveals 4.5% severe corneal edema after cataract surgery in non diabetics and 14.3% in diabetics. Thus despite the advancement in phacoemulsification and its outcome persistent corneal edema remains a significant reason of visual impairment requiring corneal graft. Therefore in our country where cataract is still a major cause of visual blindness, preoperative details of corneal endothelium will help us identify those patients who are at increased risk of postoperative corneal edema.

There is direct correlation of age with average area of the endothelial cell, our study shows steady progressive increase from 384.30±31.77 um^2 in third decade to 430.33±49.16 um^2 ($p<0.00$) in seventh decade of life. Qamar[15] and Tananuvat[18] have seen similar correlation of mean cell area with age.

Further in our study inverse correlation is seen among age and Endothelial cell Density, Co efficient of variation, hexagonality of cells (r: -0.19, $p<0.00$) (r:-0.05, $p<0.17$) (r:-0.01, $p<0.70$) respectively.

There is only one study which studied the relationship of age with all four parameters of corneal endothelial morphology in Pakistani population and we suggest further studies to have a strong database to assign normal values in our population.

Conclusion

Our study reports the normative Endothelial morphology and corneal thickness in Pakistani population at Eye department, FRPMC, this data will serve as a baseline for further studies at any department. Our study shows both Central corneal thickness and Endothelial cell density decreases with aging and no statistical difference was seen gender wise. Besides, Corneal edema remains a significant reason for visual loss following cataract surgery and thus knowledge of endothelial cell morphology will help us to identify those at increased risk and adopt safe surgical strategy.

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