Corneal Endothelial Cell Density and Morphology in Nigerians

Efeoghene U. Ani[1*], Sebastain N. N. Nwosu[2], Chinyere N. Pedro-Egbe[1], Sotonibi A. H. Cookey[1] and Elizabeth A. Awoyesuku[1]

[1]*Department of Ophthalmology, University of Port Harcourt Teaching Hospital, Rivers State, Nigeria.*
[2]*Department of Ophthalmology, Guinness Eye Centre, Onitsha, Anambra State, Nigeria.*

Authors' contributions

Article Information

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ABSTRACT

AIM: To determine the mean density and describe the morphology of corneal endothelial cells in adult Nigerians in Port Harcourt.
Study Design: A population-based cross-sectional study.
Place and Duration: A study conducted among adult Nigerians aged ≥ 18 years in Port Harcourt city Local Government Area, Rivers State, Nigeria between January and April 2014.
Methodology: Participants were selected using multi-stage cluster random sampling technique. An interviewer-based semi-structured questionnaire was administered to obtain demographic data. All participants had ocular examinations done including visual acuity measurement, anterior segment examination, fundoscopy, and non-contact specular microscopy.

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*Corresponding author: E-mail: efeudi@yahoo.com;

Results: Four hundred and eighty (n=480) subjects were studied. There were 212 males (44.2%) and 268 females (55.8%) with a mean age of 43.0±14.2 years and range 18-91 years. The mean Endothelial Cell Density (ECD) was 2791±221 cells/mm^2. Males had a tendency to have a higher ECD (2882±220 cells/mm^2) than females (2784±215 cells/mm^2, p=0.490) in ages less than 40 years.

Conclusions: The mean ECD obtained in adult Nigerians was 2791±221 cells/mm^2. No statistically significant difference was found in ECD between males and females. The degree of polymegathism of corneal endothelial cells increased with age in the study population but this was also not statistically significant (p=0.141).

1. INTRODUCTION

Endothelial cell analysis provides important information on corneal function and viability. Endothelial cell density is an acceptable measure of endothelial cell function [1]. Decisions concerning endothelial health and function in an individual should be based on normative data derived from the reference population. Therefore, it is important for populations of different racial and ethnic backgrounds to establish their own normative data on which decisions regarding endothelial function can be based. A population-based study is therefore necessary to determine this.

Endothelial cells that show a great variability in size and shape are considered to be under physiologic stress and abnormal [2]. The corneal endothelial cell wound repair is also reflected as an increase in the variation of individual cell areas, i.e. polymegathism or coefficient of variation (CV). A normal cornea is expected to have 60% of the endothelial cell as hexagons. Stress results in a decrease in the percentage of hexagonal cells. Endothelial cell morphology analysis includes: cell area, cell density, polymegathism (coefficient of variation), and pleomorphism.

Corneal endothelial cell analysis is therefore useful in identifying populations at risk of developing corneal decompensation following intraocular surgeries and in identifying potential healthy corneal graft donors in a population [3].

There are differences in endothelial parameters among various populations. Normative data regarding endothelial cell density and morphology are important as they facilitate assessment of the functional reserve of the endothelium in individual patients [4].

2. MATERIALS AND METHODS

This is a community- based descriptive cross sectional study conducted among adult residents of Port Harcourt City Local Government Area (PHALGA) of River State.

2.1 Inclusion Criteria

1. Adults ≥ 18 years and agreed to participate in this study.
2. No history of ocular surgery, trauma or wearing contact lens
3. No history of corneal disease
4. Visual acuity (VA) ≥ 6/18
5. No systemic comorbidity e.g. diabetes mellitus or hypertension

2.2 Exclusion Criteria

1. Age ≤ 18 years
2. History of intraocular surgery or trauma
3. Participants receiving medical treatment for glaucoma, hypertension and/or diabetes mellitus
4. Those who had a random blood sugar ≥ 11.1 mmol/L
5. Had vertical cup disc ratio > 0.5 or cup asymmetry of >0.2 [5]
6. Those with corneal disease
7. Those who had corneal refractive surgery
8. VA<6/18

2.3 Ethical Consideration

Ethical approval was obtained from the Ethics Committee of University of Port Harcourt Teaching Hospital. Approval was sought from the Port Harcourt City Local Government Area secretariat and permission was also obtained from the community leaders. Written informed consent was obtained from all participants.

2.4 Study Procedure

Port Harcourt City Local Government Area (PHALGA) is made up of the following 11 communities. Participants from the 11 communities were randomly selected and examined. Participants were selected through a three-stage procedure.

2.4.1 First stage

Each name of the eleven communities was written on a 2 cm by 2 cm paper which was folded and put in a bag. An assistant then picked blindly four communities after mixing the contents of the bag.

2.4.2 Second stage

Ten streets within each of the selected communities would be randomly selected from the list of streets obtained from PHALGA secretariat.

2.4.3 Third stage

Starting with the index house chosen by the flip of a coin (heads for first house right and tails for first house left), all eligible participants were invited to the study venue within the community. Enumeration was given when the target was achieved for each community.

If nobody was found eligible in the chosen household, the next eligible household would be screened.

The interviewer-administered questionnaire was administered to obtain background information of each eligible participant.

Ocular examination and specular microscopy was carried out using a non-contact specular microscope incorporating pachymeter (TYOPTICS, Tianjin Suowei Electronics Technologies LTD, Model SW-7000, China)

2.5 Endothelial Cell Density (ECD) Technique Using Specular Microscopy

The subject was asked to sit with his chin on the chin rest and forehead against the head rest. He was asked to focus on a green target presented by the instrument. The Specular microscope auto-aligns and measures the central corneal thickness and captures the image of the endothelial cells. Three images from central cornea will be taken of at least 50 contiguous cells and manually marked with a computer by the researcher. A mean of the ECD from three images of central cornea will be calculated. Two readings were taken for each eye and the average value documented.

Data obtained was analysed using Statistical Package for Social Sciences version 17 (SPSS-17).

3. RESULTS

Four hundred and eighty (480) subjects were recruited and analysed.

3.1 Age and Sex Distribution of Study Population

There were 212 males (44.2%) and 268 females (55.8%).The mean age of the study population was 43.0±14.2 years, ranged from 18 to 91 years. The mean age for males was 44.8±15.8 years and 41.6±12.7 years for females. The 31-50 years constituted more than 65% of the whole study population. Subjects aged 71-91 years constituted only 4%. There was a statistically significant difference in gender in the study population (p= 0.004) with slight female preponderance as shown in Table 1.

Table 1. Age and sex distribution of study population

Age groups in years	Male N (%)	Female N (%)	Total N (%)
≤30	43 (20.3)	45 (16.8)	88 (18.3)
31 -40	48 (22.6)	93 (34.7)	141 (29.4)
41 – 50	54 (25.5)	70 (26.1)	124 (25.8)
51 -60	38 (17.9)	37 (13.8)	75 (15.6)
61 – 70	14 (6.6)	19 (7.1)	33 (6.9)
>70	15 (7.1)	4 (1.5)	19 (4.0)
Total	**212 (44.2)**	**268 (55.8)**	**480 (100.0)**

Pearson chi-square X^2= 17.31, df=5, p = 0.004

3.2 Mean Corneal ECD

The mean corneal endothelial cell density (ECD) of the study population was 2783.0±215.4 cells/mm^2 and this varied with age and gender.

The overall mean ECD was 2784.0±218.0 cells/mm^2 in males and 2782.0±213.9 cells/mm^2 in females. Corneal ECD was higher in male than that of female in groups with age ≤ 40 years (p=0.592). ECD counts were similar between

ages 41 and 50 in both male and female participants (male=2778 cells/mm^2 vs. female =2772 cells/mm^2). Thereafter, there is a reversal of pattern that females had higher ECD than that of males. However no statistical significance was found (p=0.101).

3.3 ECD in Males and Females

The difference in ECD between males and females in various age groups is as shown in Table 2. No statistically significant difference was found in the ECD between males and females.

3.4 Relationship between ECD and Age According to Gender

Corneal endothelial cell density was found to significantly decrease with age in males and females (p<0.05 respectively) though the relationship between ECD and age was weak (r= 0.1440) see Figs. 1 and 2.
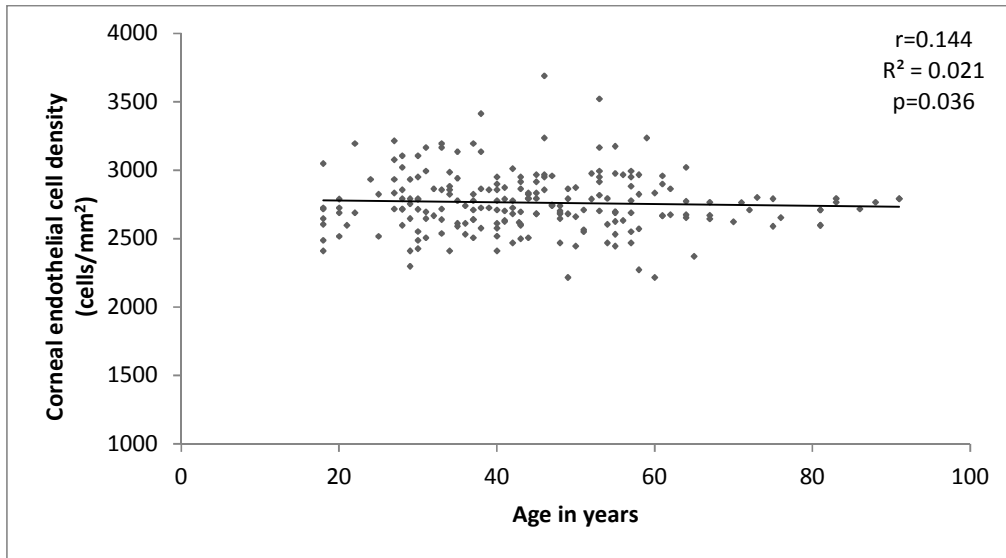
Fig. 1. Relationship between ECD and age in male
Bivariate linear regression

Fig. 2. Relationship between ECD and age in female
Bivariate linear regression

4

3.5 Relationship between Hexagonality of Endothelial Cells, Coefficient of Variation and Age in the Study Population

Fig. 3 shows that the hexagonality of corneal endothelial cells reduced with increasing age in the study population but this was not statistically significant (r=-0.079, p=0.084).

The degree of polymegathism of corneal endothelial cells was assessed by the Coefficient of Variation (CV) from expected normal size. Fig. 4 shows that coefficient of variation of corneal endothelial cells increased with aging in the study population but this was also not statistically significant (p= 0.141).

4. DISCUSSION

According to the Nigerian National Blindness and Visual Impairment Survey (2005-2007), corneal scarring and opacification accounted for 7.9% of causes of blindness in Nigeria [5]. The inability of the endothelial cells to respond efficiently to any form of trauma including surgery could be responsible for the oedema and opacification [6].
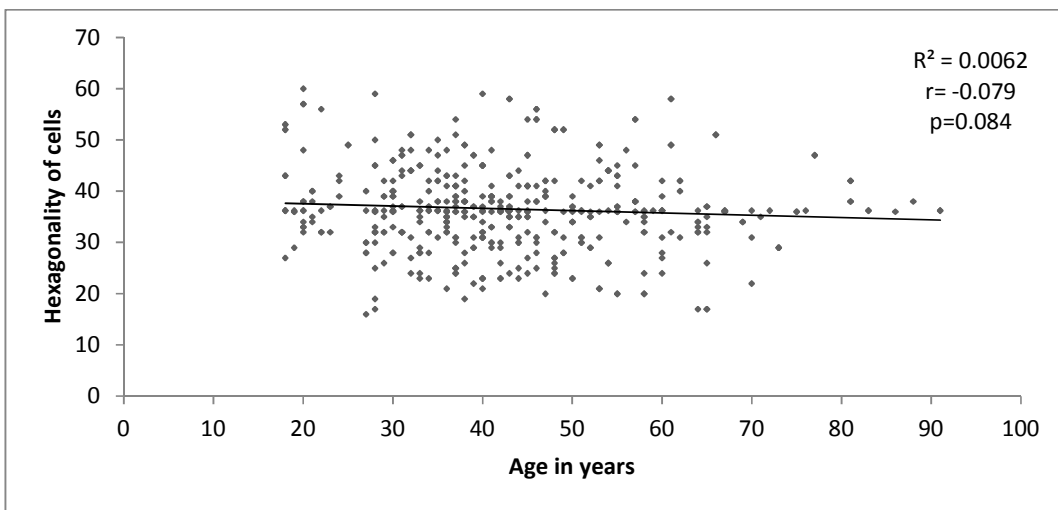

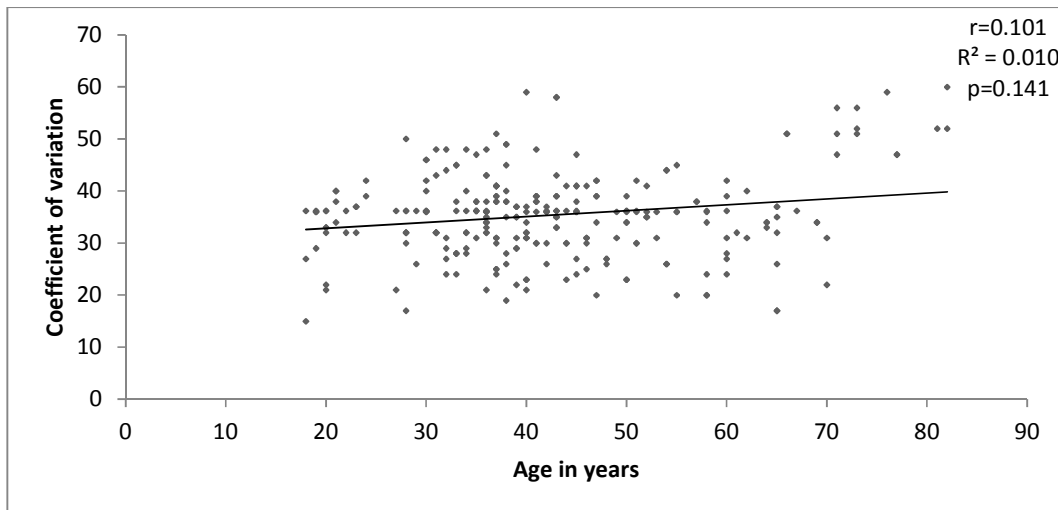**Fig. 3. Relationship between hexagonality of endothelial cells and age in study population**

Fig. 4. Relationship between coefficient of variation and age in the study population

5

Table 2. Difference in ECD between males and females in different age groups

Age groups	N	Mean ECD diff	Conf. interval of mean	t-test	p-value
<30 years	88	54.7 ±34.6	-14.1 to 123.5	1.580	0.118
31-40 years	141	22.7±42.3	-60.9 to 13.4	0.537	0.592
41-50 years	124	5.6±39.6	-72.8 to 84.1	0.143	0.887
51-60 years	75	-21.8±52.6	-126.7 to 83.7	-0.415	0.679
61-70 years	31	- 62.8±89.9	-246.3 to120.7	-0.698	0.490
>70 years	19	-28.6±47.4	-128.6 to 71.4	-0.603	0.554

Independent t-test was used for analysis

In a study on 537 normal Indian eyes by Rao et al. [7], the mean ECD in the study population was reported as 2525±337 cells/mm^2. The South Asian study of three ethnic groups by Snellingen et al. [8] showed that mean corneal ECD was significantly different in the three ethnic populations (Between the three patient populations mean cell density varied from 2634 cells/mm^2 in western Nepal to 2714 cell/mm^2 in Southern Indian and 2782 cells/ mm^2 in southern Bangladesh (p = 0.0001). An Iranian study(4) on normal eyes showed a far less mean endothelial cell density of 1961±457 cells/mm^2. Mohd [9], in his study of 125 normal Malay Eyes reported a mean endothelial cell density of 2648 cells/mm².

A comparison of ECD in the American, Japanese and Indian, Chinese and Iranian populations revealed that the Japanese have the highest values of ECD [7,10]. The higher ECD in the Japanese population could account for the lower incidence of bullous keratopathy in the Japanese population [10].

It is clear that significant differences in corneal endothelial properties do exist among races and ethnic groups.

Salih et al. [9] in their study of normal Malay Eyes reported a slight difference in ECD between males and females, this difference was however not statistically significant. This result was similar to results reported in Chinese, American and Japanese eyes [10]. On the contrary, differences in endothelial cell density between genders were found to be significant in Filipino eyes. Results showed that women had a MCD 7.8% greater than men [11]. A similar pattern but lower percentage difference (2.9%) was observed in South Asian females [8].

Although several studies have reported a clear inverse relationship between ECD and age in normal populations [7,12] other investigators have stated that there is no significant correlation between ECD and age in populations aged 40 years and above [13] Padilla et al. [14] showed

that there was a definite trend toward decreasing ECD with increasing age up to the sixth decade of life, a reverse trend was noted at 61years and above in Filipinos. Ropper Hall et al. [15] in Birmingham, UK described a mean cell count for each decade that gradually declined up to the age of 50 but showed no appreciable difference thereafter. Studies by Bourne and Kaufman (who did initial work with the non-contact specular microscope) noted a statistically significant decrease in the number of central endothelial cells with age [16]. Other studies agreed with the negative correlation of ECD with age [4,11]. In a study on eyes of Indian population by Rao et al. [7] the rate of cell loss was reported as 0.3% per year. This is in agreement with other studies that had cell loss rate between 0.3%-0.5% [17,18]. In longitudinal studies in which some subjects were examined again at a later date, a higher annual loss rate was reported up to 2.5% per year [19].

The mean ECD obtained in this study was 2783.0±215.4 cells/mm^2. The mean endothelial cell density in this study was similar to that described for other African countries. Values in this study are close to values obtained in Indian eyes (2782 ±250 cells/mm^2) [7] but slightly higher than reported for Nigerians (2693±309 cells/mm^2) scheduled to undergo cataract surgery for senile cataract [20]. Factors including age and the presence of cataract could account for this difference. The Japanese still remain the population with the highest reported endothelial density (3893±259 cells/mm^2). The lower incidence of pseudophakic bullous keratopathy in Japanese eyes may be due to their higher endothelial cell density [10]. Accordingly, the relatively lower endothelial cell counts in eyes of Nigerian population may predispose this population to an increased risk of pseudophakic bullous keratopathy.

Males were noted to have higher endothelial cell density than females in those less than 40 years old, but lower in those aged above 40 years (Fig. 2). This pattern was however not statistically significant. The reason for this reversal is not

readily apparent but may be due to the higher rate of decline of corneal endothelial cells in females. It could also be associated with hormonal differences but this is subject to further research. Other studies show varying results; in Filipinos, females are reported to have higher ECD values than males and a slight increase with age up to 40 years before a slight decline with age in both genders [4]. Pallida reported a similar trend but up to the age of 60 years with a decline afterwards [14]. Others however showed no variability with age [8]. Although investigators differ in their findings about the relationship between age and gender to endothelial characteristics, it is clear that significant differences in corneal endothelial properties exist among different races and ethnic groups [4].

Endothelial cell density in this study was found to significantly decrease with age. The results of this study has shown that with increasing age there is a general trend toward decreased ECD, decreased hexagonality, and increased polymegathism (CV). These findings are in agreement with many previous studies [7,4,12]. This study confirms previous reports [21] that ECD correlates with age and that endothelial cell count decreases with increasing age.

5. CONCLUSION

The mean ECD in age matched male and female of Nigeria were similar. However, significant decrease of ECD was found to be associated with aging.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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