Normal corneal endothelial morphology of healthy Saudi children aged 7–12 years

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Purpose

The aim of this study was to describe the corneal endothelial morphology of healthy Saudi children aged 7–12 years and investigate variations on the basis of age and sex.

Participants and methods

In this prospective study of 412 healthy children, one eye was examined of each child. The endothelial cell density (ECD), percentage coefficient of variation (CV), and cell hexagonality (Hex) were determined using a noncontact Nidek CEM 530 specular microscope. An unpaired *t*-test was used to compare ECD measurements between boys and girls. Descriptive statistics of endothelial characteristics (ECD, CV, Hex) of the right eyes of the children at each age were analyzed for the entire sample using Kruskal–Wallis and Spearman's correlation tests.

Results

The Kruskal–Wallis test showed statistically significant differences in ECD on the basis of age ($P = 0.01$) and Spearman's correlation test detected a weak negative correlation between ECD and age (–0.20, $P = 0.0001$). Analysis of the CV did not indicate any statistically significant differences with age ($P = 0.98$), but a weak positive correlation was detected between CV and age ($r = 0.02$, $P = 0.69$). No significant differences in Hex were observed at each age ($P = 0.10$), but a weak negative correlation was detected between Hex and age ($r = -0.14$, $P = 0.001$).

Conclusion

In children, ECD decreases with increasing age whereas CV and Hex do not change significantly with age.

Keywords:

cell hexagonality, endothelial cell density, Nidek CEM 530 specular microscope, noncontact, percentage coefficient of variation

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Introduction

The primary function of the corneal endothelium is to maintain optical transparency of the cornea [1]. It is well documented that the corneal endothelium has a limited capacity for repair. It compensates for lost cells by extending endothelial cells to cover the posterior corneal surface, causing a gradual increase in the size of the cells and resulting in increased cellular pleomorphism and a decrease in the proportion of polymorphic cells with age [2,3]. Quantitative analysis of endothelial cell parameters is essential not only to determine the normal range at each age but also to study normative data among various populations [4–6].

The recent introduction of new noncontact specular microscopes such as the Nidek CEM 530 specular microscope has facilitated the measurement of mean values for endothelial cell density (ECD), percentage coefficient of variation (CV), and cell hexagonality (Hex). The main advantage of the Nidek CEM 530 specular microscope is that it is easy to use with children for the study of ECD, CV, and Hex.

Several studies have reported different ECD parameters among Indian, Filipino, Japanese, American, and Chinese populations [5,7–9]. Thus, investigation of ECD parameters in a population of healthy children is important as this information is relevant to the clinical care of patients as well as for use in research studies. To the best of our knowledge, no such data are available for children in Saudi Arabia, and this prospective study is the first to report on the characteristics of endothelial cells in the eyes of healthy Saudi children and to describe the rate of endothelial cell loss with increasing age.

The aim of this study was to describe the corneal endothelial morphology of healthy Saudi children aged 7–12 years and investigate variations on the basis of age and sex.

Participants and methods

A total of 412 children were selected randomly from a school population in Riyadh, Saudi Arabia; their ages ranged from 7 to 12 years. Comprehensive anterior segment examinations of all children were performed

using a slit-lamp biomicroscope. Exclusion criteria were the use of contact lenses, the presence of dry eye or ocular trauma, a history of ocular surgery or intraocular abnormalities, a family history of a hereditary corneal disorder, increased intraocular pressure, uveitis, corneal opacity, evidence of endothelial dystrophy on slit-lamp biomicroscopy, and any systemic disease, such as diabetes mellitus [10]. Spherical and cylindrical refractions and intraocular pressure were determined by autorefractometry (Auto Kerato-Refracto-Tonometer TRK-1P; Topcon Inc., Tokyo, Japan). A single investigator performed all measurements of ECD, CV, and Hex. All measurements of ECD, CV, and Hex were performed using the noncontact Nidek CEM 530 specular microscope (Nidek Co., Tokyo, Japan). The purpose of the study was explained to the parents of all children and informed consent was obtained from each parent before the examination. The study was carried out in conformance with the ethical considerations in the 2008 Declaration of Helsinki, and the study protocol was approved by the research ethics review board of the College of Applied Medicine Science at King Saud University.

Noncontact specular microscopy method

The noncontact Nidek CEM 530 specular microscope was used as described below. Only the right eye of each participant was measured as previous studies have reported no significant difference between eyes in the same individual [11,12]. The participants' head was positioned against the head band and chin rest, and they were then instructed to look straight ahead at the fixation targets. Pictures were captured of the central cornea area. Each image was taken after proper positioning of the alignment dot, circle, and bar on the screen. Endothelial cell morphology analyses were carried out using automated measurements with the retracing method using the manufacturer's built-in image analysis software. The mean ECD, CV, and Hex values were calculated automatically. The images were printed with the analyzed data.

Statistical methods

The data for all children were collected and analyzed using Microsoft Excel 2007 (Microsoft Corporation, Redmond, WA, USA) and Medcalc software (version 11.4.4.0, bvba, ostend, Belgium). An unpaired *t*-test was used to compare ECD measurements between boys and girls. Descriptive statistics of the endothelial characteristics (ECD, CV, Hex) of the right eyes of the participants at each age were analyzed using Kruskal–Wallis and Spearman's correlation tests. All tests were two tailed. The level of statistical significance was set at 0.05.

Results

The characteristics of the children are summarized in Table 1. There was no statistically significant difference in the mean ECD measurement between boys and girls in the *t*-test analysis (Table 2). The ECD measurements decreased rapidly with age in a nonlinear pattern until age 10 years. None of the children had an ECD value below 2300 cells/mm^2 at any age. The Kruskal–Wallis analysis showed statistically significant differences in ECD among the different ages (P = 0.01) and the Spearman's correlation findings showed a weak negative correlation between ECD and age (Table 3). Figure 1 shows the decrease in ECD values with age.

For the CV, the Kruskal–Wallis analysis did not detect any statistically significant differences in CV among

Table 1 Age and refractive errors for the studied population

Characteristics	Mean ± SD	Range
Age (years)	9.50 ± 2.00	7–12
Refractive error	−1.25 ± 0.75 D	−0.50 to −3.00 D

Table 2 Differences in the ECD values according to sex

Gender	Number of eyes	ECD (cells/mm^2)[a]	Range	Unpaired (*P* value)
Boys	208	3162.89 ± 207.97	2314–3784	0.18
Girls	204	3190.60 ± 207.65	2342–3881	

ECD, endothelial cell density; [a]Mean ± SD.

Table 3 Endothelial characteristics (ECD, CV, Hex) of the right eye at each age

Age (years)	Number of participants	ECD (cells/mm^2)	CV (%)	Hex (%)
7	74	3243.92 ± 229.32	22.50 ± 2.28	70.20 ± 3.98
8	74	3214.50 ± 211.75	22.35 ± 2.17	69.81 ± 3.02
9	82	3165.28 ± 210.19	22.43 ± 2.35	69.74 ± 3.52
10	67	3142.78 ± 187.51	22.43 ± 2.05	69.63 ± 3.55
11	56	3138.04 ± 183.94	22.46 ± 2.15	68.82 ± 3.47
12	59	3134.92 ± 196.31	22.54 ± 2.28	68.63 ± 2.95
Total		3176.50 ± 208.03	22.45 ± 2.21	69.53 ± 3.47
Range		2314–3881	17–29	60–80
Significance for intergroup difference[a]		0.01	0.98	0.10
Correlation (r, P)[b]		(−0.20, 0.0001[†])	(0.02, 0.69[†])	(−0.14, 0.001[†])

CV, coefficient of variation; ECD, endothelial cell density; Hex, hexagonality; [a]Kruskal–Wallis; [b]Spearman's correlation; [†]Correlation significant at a *P* value of 0.05 (two tailed).

the different ages ($P = 0.98$), but Spearman's correlation analysis showed a weak correlation between CV and age (Table 3). Figure 2 shows how the CV increased with age. No statistically significant differences in Hex were detected among the different ages ($P = 0.10$), but the Spearman's correlation analysis did show a weak correlation between Hex and age (Table 3). Figure 3 shows how Hex decreased with age. The endothelial cell morphology characteristics of the children are summarized in Table 3.

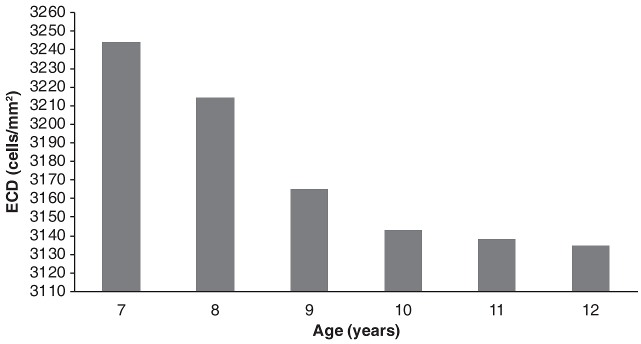
Discussion

Studies assessing the corneal endothelium have confirmed that ECD values just after birth or in infancy (>4200 cells/mm^2) are higher than those in children (3160 cells/mm^2) and young adults (2929.94 cells/mm^2). These studies have shown that there is a common trend toward a decrease in ECD with age [3,4,11–14].

In the present study, the mean ECD decreased rapidly in a nonlinear pattern until age 10 years. No statistically significant difference in ECD was observed between boys and girls, which supports findings from other studies [4,14,15]. However, a statistically significant difference in ECD was observed between children of different ages ($P = 0.01$) and a weak negative correlation was detected between ECD and age. No statistically significant differences in CV or HEX were detected between children of each age ($P = 0.98$), but there was a weak positive correlation between CV and age and a weak negative correlation between Hex and age. Jorge *et al.* [15] reported that ECD and Hex decreased with increasing age, but CV increased with age; also, the ECD had a strong negative correlation, Hex showed a weak negative correlation, and the CV showed a weak correlation. The difference between the findings of our study and theirs may be because of racial characteristics or the wide age range used in their study. In contrast, Hiles *et al.* [16] reported no statistically significant difference in ECD among individuals aged 5–20 years. This could be because of the presence of refractive errors and inhomogeneity.

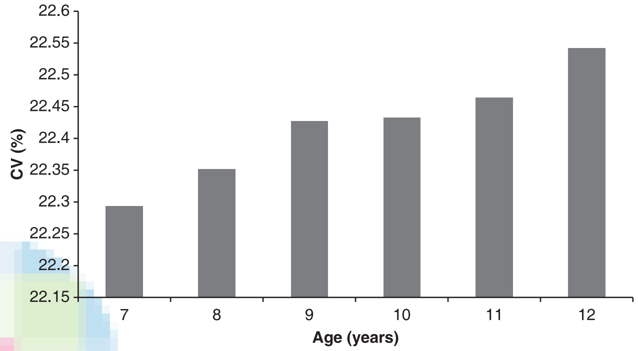
Certainly, there have been a few studies of ECD in children [3,4,11,12], but the majority do not report details of CV and Hex (Table 4). Jorge *et al.* [15]

Figure 1



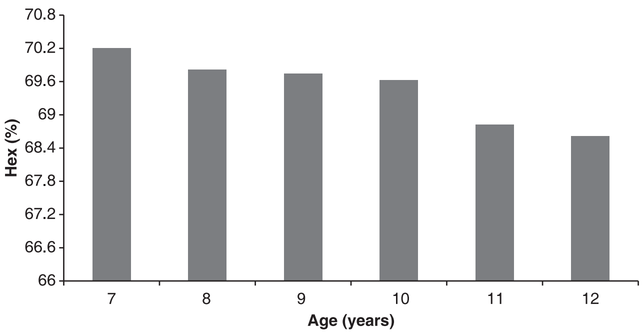
Endothelial cell density as a function of age. ECD, endothelial cell density.

Figure 2



The coefficient of variation as a function of age. CV, coefficient of variation.

Figure 3



Endothelial cell hexagonality as a function of age. Hex, hexagonality.

Table 4 Summary of corneal endothelial cell density and other morphological characteristics in children reported in multiple studies

References	Ages of children (years)	Number of eyes	ECD mean (cells/mm²)	Range of ECD values (cells/mm²)	CV (%)	Hexagonality (%)
Bourne and Kaufman [3]	6–11	40	3150	2950–3250	–	–
Bigar [11]	5–11	55	3581	3067–4171	–	82
Nucci *et al.* [4]	5–14	214	3160	2597–3981	–	–
Speedwell *et al.* [12]	5–11	36	3987	2627–5316	28.20	66.6
This study	7–12	412	3174.53	2314–3906	22.45	69.53

CV, coefficient of variation; ECD, endothelial cell density.

reported CV values for children aged 0–9 and 10–19 years of 31.00 ± 2.00 and 62.50 ± 3.32%, respectively, and Hex values of 31.00 ± 4.00 and 58.44 ± 7.04%, respectively. Differences between their findings and those of our study are probably because of the different age ranges used as well as the different racial backgrounds [14].

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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