Original Article

Myopia severity and corneal endothelium: morphological variations across low, moderate, and high myopia

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ABSTRACT

Background: Myopia, a condition of growing concern in Asian populations, has been linked to ocular structural changes that may affect corneal endothelial morphology. Endothelial cell density (ECD), shape, and size changes have been observed in cases of high myopia. However, population-specific data, particularly in Malaysia, remain limited. In this study, we evaluated corneal endothelial morphology across different severities of myopia in young Malaysian adults.

Methods: For this cross-sectional study, we categorized individuals with myopia, aged 19–24 years, attending the International Islamic University Malaysia Optometry Clinic, into low, moderate, and high myopia groups, based on spherical equivalent. They underwent non-cycloplegic refraction, axial length, intraocular pressure, and slit-lamp assessments. Using a non-contact specular microscope, we measured corneal endothelial parameters, ECD (cells/mm²), coefficient of variation (CV) of the cell area, percentage of hexagonal cells (HEX, %), and central corneal thickness (CCT, μm) centrally, in triplicate, and averaged the values. All assessments were conducted by an experienced optometrist under controlled environmental conditions.

Results: We analyzed data from 374 eyes of 187 young adults (mean [standard deviation] age: 20.16 [0.75] years) across varying degrees of myopia. Axial length increased with myopia severity, while best-corrected visual acuity remained comparable among groups. Statistically significant differences in mean ECD, CCT, and HEX (all $P < 0.05$), but not in CV, were observed across the three myopia groups. Post-hoc analysis revealed that, compared to low myopia, the high myopia group had significantly lower ECD, HEX, and CCT (all $P < 0.05$), while the moderate myopia group showed significantly reduced ECD and HEX (both $P < 0.05$). ECD, CCT, and HEX did not differ significantly between the moderate and high myopia groups (all $P > 0.05$).

Conclusions: We demonstrated that higher myopia severity in young Malaysian adults was significantly associated with lower ECD, reduced HEX, and thinner CCT, whereas CV did not differ across myopia levels. These findings indicated that increasing myopia severity is associated with notable morphological changes in the corneal endothelium. Thus, progressive axial elongation in myopia may adversely impact corneal endothelial morphology and biomechanical stability. Given the cross-sectional nature and limited demographic scope of the study, further longitudinal and multi-ethnic studies are warranted to clarify the causal pathways and long-term implications of myopia-related endothelial changes.

KEYWORDS

myopias, cornea, endothelial cell, endothelial cell density, central corneal thickness, hexagonal cells, specular microscope, malaya, adults

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INTRODUCTION

Myopia, also termed short- or near-sightedness, is a common refractive error that may develop due to genetic or environmental factors. Its prevalence in Asian populations has been steadily increasing over the past few decades [1-3]. The condition is associated with elevated risks of various ocular abnormalities, including abnormal axial elongation and excessive retinal, choroidal, and scleral stretching. These biomechanical changes, which occur as the eye elongates during myopia progression, may also affect the morphology and function of the corneal endothelium [4].

As global myopia rates are escalating, the relationship between myopia severity and corneal endothelial health has increasingly gained attention. The corneal endothelium, a monolayer of hexagonal cells lining the posterior corneal surface, plays a critical role in maintaining corneal transparency by regulating stromal hydration [4-6]. Changes in endothelial structure or function can have significant implications for corneal integrity and vision quality. Previous studies have reported that highly myopic eyes often demonstrate endothelial morphological changes, particularly reduced endothelial cell density (ECD), which has been linked to increased axial length (AL) and decreased central corneal thickness (CCT) [4-6]. These findings suggest that the biomechanical stress associated with axial elongation may negatively impact endothelial health.

Beyond cell density, morphological features, such as pleomorphism (variation in cell shape) and polymegathism (variation in cell size) have also been investigated in relation to myopia [6-8]. High myopia has been associated with increased pleomorphism and polymegathism, potentially indicating compromised endothelial function. These alterations may be further influenced by external factors common among individuals with myopia, such as long-term contact lens wear or a history of refractive surgery. Additionally, myopia-associated corneal thinning may alter the biomechanical properties of the cornea, potentially influencing endothelial stability and increasing susceptibility to ocular complications [5, 6, 9, 10].

Population-specific data on corneal endothelial characteristics remain scarce. Despite these insights, research on corneal endothelial morphology in the Malaysian population remains limited. In this context, significant gaps exist in the understanding of how endothelial parameters vary with environmental, racial [6], and clinical factors. Therefore, in this study, we investigated the relationship between corneal endothelial morphology and varying degrees of myopia in a young adult Malaysian population.

METHODS

For this cross-sectional study, we recruited consecutive individuals with myopia, aged 19–24 years, who attended the International Islamic University Malaysia (IIUM) Optometry Clinic between September 2022 and June 2023. The study was approved by the IIUM Research Ethics Committee and was conducted in accordance with the tenets of the Declaration of Helsinki. All participants were thoroughly briefed on the procedures, and written informed consent was obtained prior to data collection.

Individuals with myopia but with otherwise healthy eyes, who wore spectacles for vision correction, were included in the study. Based on the spherical equivalent (SEQ) of manifest refraction, participants were categorized into three groups: low myopia (–0.50 D to –2.75 D), moderate myopia (–3.00 D to –5.75 D), and high myopia (–6.00 D and above) groups [11, 12]. The exclusion criteria included the presence of ocular surface abnormalities or diseases, such as superficial punctate keratitis, recurrent pterygium, corneal opacity, or corneal irregularity; current contact lens wear; use of artificial tears; and eyes in which corneal topography could not yield reproducible measurements due to central corneal obstruction by pterygium [13, 14].

Refractive error was measured using standard optometry, including non-cycloplegic refraction, with best-corrected distance visual acuity (BCDVA) assessed by means of a logarithm of the minimum angle of resolution (logMAR) chart and recorded in logMAR notation. Anterior segment examination was performed using a digital slit-lamp biomicroscope (Model HR-Elite Mega Digital Vision, CSO, Scandicci-Firenze, Italy) with white light diffused illumination, while posterior segment examination was performed under a slit-lamp along with an auxiliary non-contact lens. AL was measured using the IOLMaster 700, a swept-source optical coherence tomography-based biometer (Carl Zeiss Meditec, Dublin, CA, USA). Intraocular pressure was assessed using a Topcon CT-80 non-contact tonometer (Topcon Corp., Tokyo, Japan). All assessments were conducted by an experienced optometrist between 9:00 and 11:00 AM to minimize diurnal variation, in the same examination room. Room temperature and humidity were maintained consistently at 20–24°C and 40–50%, respectively.

A non-contact specular microscope (CEM-530; Nidek Corp., Ltd., Gamagori, Japan) was used to assess ECD (cells/mm^2), coefficient of variation (CV) of the cell area, percentage of hexagonal cells (HEX, %), and CCT (μm). All measurements were taken at the central cornea. For each parameter, three consecutive measurements were recorded to ensure reliability, and the average value was used in data analysis. All measurements were performed in automatic mode by one experienced optometrist.

All statistical analyses were performed using SPSS Statistics for Windows (version 25.0, IBM Corp., Armonk, NY, USA). The normality of data distribution was evaluated using the Shapiro–Wilk test. Quantitative variables are described using mean and standard deviation (SD) and qualitative variables are summarized using number (percentage). The ECD, CV, CCT, and HEX were compared between low, moderate, and high myopia groups by using one-way analysis of variance with Tukey's post-hoc analysis for pairwise comparisons. Statistical significance was set at $P < 0.05$.

Table 1. Comparing corneal endothelial cell morphology, BCDVA, and AL in different severity of myopia

Variables	Degree of myopia				P_1-value
	All participants (n = 374)	Low Myopia (n = 120)	Moderate Myopia (n = 120)	High Myopia (n=134)	
ECD (cells/mm²), Mean ± SD	3098.94 ± 235.66	3185.03 ± 123.83	3058.94 ± 215.80	3032.55 ± 177.54	**0.001**
P-value for Pairwise Comparison	**P_2-value = 0.025**; **P_3-value = 0.001**, P_4-value = 0.134				
CV (%), Mean ± SD	26.84 ± 2.54	28.00 ± 2.87	26.18 ± 3.04	26.33 ± 5.40	0.121
CCT (µm), Mean ± SD	556.24 ± 27.54	566.18 ± 29.98	552.58 ± 29.23	549.58 ± 22.18	**0.036**
P-value for Pairwise Comparison	P_2-value = 0.235, **P_3-value= 0.001**, P_4-value = 0.254				
HEX (%), Mean ± SD	64.7 ± 3.1	67.4 ± 4.6	63.4 ± 2.6	62.5 ± 3.6	**0.001**
P-value for Pairwise Comparison	**P_2-value = 0.036**; **P_2-value= 0.001**, P_3-value= 0.374				
BCDVA (logMAR), Mean ± SD	0.10 ± 0.08	0.09 ± 0.08	0.10 ± 0.04	0.10 ± 0.06	0.245
AL (mm), Mean ± SD	23.75 ± 0.42	22.34 ± 0.45	23.55 ± 0.35	25.42 ± 0.63	**0.001**

Abbreviations: n, numbers; ECD, endothelial cell density; cells/mm², cells per square millimeter; SD, standard deviation; CV, coefficient of variation of the cell area; CCT, central corneal thickness; µm, micrometer; HEX, percentage of hexagonal cells; BCDVA: best-corrected distance visual acuity; logMAR; logarithm of the minimum angle of resolution; AL, axial length; mm, millimeter. Note: *P*-values < 0.05 are shown in bold; P_1 represents the *P*-value from a one-way repeated-measures (ANOVA) comparing the three levels of myopia severity; P_2, P_3, and P_4 are *P*-values derived from post-hoc pairwise comparisons using Tukey's test: P_2 compares low myopia with moderate myopia; P_3 compares low myopia with high myopia; and P_4 compares moderate myopia with high myopia.

RESULTS

In total, 374 eyes of 187 individuals with myopia, who were otherwise healthy, were included in the analysis. The mean (SD) age of participants was 20.16 (0.75) years (range: 19–24 years). The group comprised 92 men (49.2%) and 95 women (50.8%). The mean SEQ differed significantly across the three myopia severity groups ($P < 0.05$). The mean (SD; range) SEQ was –1.53 D (0.69; –0.50 to –2.75 D) for the low, –4.02 D (0.84; –3.00 to –5.75 D) for the moderate, and –6.78 D (0.61; –6.00 to –8.00 D) for the high myopia group. AL showed a clear increasing trend with greater myopia severity ($P < 0.05$). The mean (SD) AL measurements were 22.34 (0.45) mm, 23.55 (0.35) mm, and 25.42 (0.63) mm for the low, moderate, and high myopia groups, respectively. In contrast, BCDVA did not significantly differ across the groups ($P > 0.05$).

Analysis of corneal endothelial cell parameters across different degrees of myopia revealed distinct trends. Eyes with high myopia demonstrated lower mean (SD) values for the ECD and CCT, measuring 3032.55 (177.54) cells/mm² and 549.58 (22.18) µm, respectively, while eyes with low myopia exhibited higher values, at 3185.03 (123.83) cells/mm² and 566.18 (29.98) µm, respectively. For the CV in cell area, the moderate myopia group had the lowest mean (SD) value, at 26.18 (3.04), while the low myopia group had the highest value, at 28.00 (2.87). However, these differences were not statistically significant ($P > 0.05$). Regarding HEX, high myopic eyes showed the lowest mean (SD) value at 62.5% (3.6%), whereas low myopic eyes had the highest HEX value, at 67.4% (4.6%) (Table 1).

The mean ECD, CCT, and HEX differed statistically significantly across the three myopia groups (all $P < 0.05$), whereas the CV did not differ significantly ($P > 0.05$). Post-hoc pairwise comparisons indicated that the mean ECD was significantly lower in both moderate and high myopia groups than in the low myopia group (both $P < 0.05$), while no significant difference was observed between the moderate and high myopia groups ($P > 0.05$). Similarly, the mean HEX was significantly reduced in the moderate and high myopia groups as compared to the low myopia group (both $P < 0.05$), with no significant difference between the moderate and high myopia groups (both $P > 0.05$). For the CCT, a significant reduction was noted in the high myopia as compared to the low myopia group ($P < 0.05$), while values did not differ statistically significantly between the low and moderate myopia, or between the moderate and high myopia groups (both $P > 0.05$) (Table 1).

DISSCUSSION

Our results revealed significant variations in corneal endothelial structure in young Malaysian adults with myopia, depending on the myopia severity. In highly myopic eyes, ECD, HEX, and CCT demonstrated notable decreases. These changes suggest that greater myopia severity may lead to structural alterations in the corneal endothelium, which are likely due to biomechanical stress caused by axial elongation. Recognizing these changes is important for improving clinical strategies in myopia care and for preserving corneal health over time.

Norhani et al.'s study [15] explored corneal endothelial morphology and its association with AL in Malaysian children of Chinese ethnicity (aged 8–9 years) who had myopia. They observed a significant reduction in the ECD and HEX values in higher myopic eyes than in emmetropic eyes. The CV increased with AL, reinforcing the notion that axial elongation may

contribute to endothelial stress. A predictive model indicated that, for every 1-mm increase in AL, the ECD decreased by 73.27 cells/mm², HEX decreased by 2.32%, and the CV increased by 1.75%. These findings provide a reference point for myopia-related endothelial changes in young children [15]. While that study [15] assessed endothelial changes in early myopia development [15], our study investigated endothelial morphology in young adults and covered a broader range of myopia severity. While both studies reported a reduction in the ECD and HEX with increasing myopia [15], suggesting that myopia-induced axial elongation negatively impacts endothelial health, our study extended this pattern to high myopia, revealing even more pronounced reductions in the ECD (3032 cells/mm²) and HEX (62.5%) in high than in low myopia categories. A key difference between the studies is the predictive model of Norhani et al., which quantified endothelial changes per mm increase in AL [15]. While our study did not provide a similar model, our findings aligned with the concept that greater axial elongation corresponded with reductions in the ECD and HEX. Additionally, while Norhani et al. [15] found that the CV of the cell area increased significantly with AL, our study showed no significant CV differences across myopia groups, suggesting potential age-related differences in endothelial adaptation to biomechanical stress. Overall, these findings indicate a continuum of endothelial changes from childhood to adulthood, reinforcing the importance of early monitoring and intervention strategies for myopia progression and its ocular implications.

Delshad and Chun [7] investigated corneal endothelial morphology in young Malaysian Chinese adults with low and moderate myopia, by using non-contact specular microscopy. They revealed that eyes with moderate myopia exhibited significantly lower ECD and HEX values than those observed in eyes with low myopia. However, no significant differences were observed in the CV of the cell area between the two groups [7]. These results suggested that increasing myopia severity may be associated with compromised endothelial integrity. While Delshad and Chun focused on low and moderate myopia [7], our study extended this analysis to include high myopia, uncovering further reductions in both the ECD and HEX with greater myopia severity. Notably, the ECD values reported by Delshad and Chun for low myopia (3063 cells/mm²) [7] closely aligned with those in our low myopia group (3185.03 cells/mm²); similarly, their findings for moderate myopia (2961 cells/mm²) [7] were comparable to those in our moderate myopia group (3058.94 cells/mm²). Our high myopia cohort showed a significant additional decline in the ECD and HEX, reinforcing the hypothesis that axial elongation and its associated biomechanical stress may contribute to progressive endothelial changes.

Consistent with Delshad and Chun's observation of a lack of significant differences in the CV of the cell area between cases of low and moderate myopia [7], we also found no statistically significant variation in the CV across all degrees of myopia. This supports the notion that variability in endothelial cell size may be less affected by myopia severity [7] and more influenced by aging, as previously suggested by Yunliang et al. [16].While both Delshad and Chun's study [7] and our current study emphasize the detrimental impact of increasing myopia severity on corneal endothelial health, our research broadens the scope by including cases of high myopia and highlighting the pronounced endothelial alterations associated therewith. These insights underscore the need for continued investigation into endothelial stability in the context of progressive myopia.

A large-scale study of corneal endothelial morphology in healthy Chinese eyes (n = 1329) reported normative values of endothelial cell parameters, including the ECD, cell area, CV of cell area, and HEX. The study found a significant decline in the ECD and HEX with increasing age, while the cell area and CV increased significantly with age. These findings provide a baseline for understanding age-related endothelial changes in a healthy population [16]. While Yunliang et al. [16] observed an age-related decline in the ECD and HEX, we revealed a significant reduction in these parameters in highly myopic eyes as compared to those with less severe myopia. Notably, the mean ECD in high myopia cases (3032 cells/mm²) was comparable to Yunliang et al.'s reported population-wide mean (2932 cells/mm²) [16]; nevertheless, our results indicate significant variation based on refractive status, rather than on age [16] alone.

Mutwaly et al. [17] in a prospective study evaluated corneal endothelial morphology and CCT in young Sudanese individuals with myopia. They revealed a significant reduction in the ECD and CCT with increasing myopia severity. Corneal guttata was observed in 9.1% of low myopia cases, but increased dramatically to 68.2% in cases of moderate myopia, suggesting progressive endothelial degeneration with increasing myopia severity. Polymegathism and pleomorphism were more prevalent in high myopia cases, indicating structural instability. A significant negative correlation was found between myopia severity and both the CCT and the ECD, reinforcing the biomechanical impact of axial elongation on endothelial integrity [17]. While Mutwaly et al.'s study highlighted endothelial degeneration in myopia [17], our study provided a broader assessment of endothelial morphology across varying degrees of myopia in a different population. Both studies [17] reported a significant reduction in endothelial parameters with increasing myopia severity, supporting the association between axial elongation and corneal endothelial changes. However, a key distinction was the presence of corneal guttata in Mutwaly et al.'s study [17], which was not observed in our study. This may suggest ethnic or environmental differences in endothelial susceptibility [18-21] or may highlight variations in underlying biomechanical stress responses.

Additionally, Mutwaly et al.'s study [17] found that the mean differences in the ECD, HEX, and CV in low, moderate, and high myopia cases were not statistically significant. In the current study, we observed a significant decline in the ECD and HEX with increasing myopia, but did not find significant differences in the CV of the cell area. This reinforced the concept that myopia primarily affects the ECD and morphology, rather than the cell size. In terms of the CCT, both studies reported a decrease in the CCT with myopia severity. Mutwaly et al.'s study [17] observed mean CCT values of 500.50 μm in low myopia and 477.87 μm in high myopia cases, whereas our study found CCT values of 566.18 μm for low myopia and 549.58

μm for high myopia cases. Despite differences in absolute values [17], the trend of corneal thinning with increased myopia severity was consistent between studies [17]. These findings demonstrate the widespread impact of myopia progression on corneal endothelial health across diverse populations. Future studies incorporating longitudinal designs and genetic analyses may help clarify population-specific variations and may refine clinical management strategies for highly myopic eyes.

Additionally, while Yunliang et al. [16] demonstrated an increasing trend in the cell area and CV of cell area with aging [16], we found no significant difference in the CV among myopia groups. This suggested that endothelial cell variability may be more influenced by aging processes than by refractive error. The HEX values reported by Yunliang et al. [16] (mean 59%) were generally lower than those observed in our low myopia group (67.4%), reinforcing the possibility that less myopic eyes of younger individuals may retain a more stable endothelial cell morphology. Together, these findings highlight distinct patterns of endothelial change—one associated with aging, as observed by Yunliang et al. [16], and the other linked to progressive myopia, as revealed by our study. Further research incorporating longitudinal analyses may clarify the interplay between age-related and biomechanical influences on endothelial integrity.

Our findings align partially with Aketa et al.'s population-based cross-sectional study in 5713 Japanese adults (2331 males and 3382 females) [8], which investigated the association between myopia and corneal endothelial morphology. Similar to our results, Aketa et al. [8] observed that high myopia was associated with significant endothelial morphological changes, particularly reduced HEX [8]. They did not find a significant association between the SEQ and ECD, nor did they observe any meaningful relationships between the SEQ and endothelial parameters in male participants [8]. Our study of young Malaysian adults found a significant reduction in the ECD and HEX with increasing myopia severity as shown overall, suggesting a more generalized endothelial susceptibility to myopia-related axial elongation. The discrepancy in the ECD findings between the studies [8] may be attributed to differences in study population age [22-25], sex ratio [26], ethnicity [19, 27], and inclusion criteria [8]: our sample comprised younger adults without current contact lens use, potentially minimizing confounding factors, such as contact lens-induced endothelial stress [28-30]. Furthermore, while Aketa et al. [8] adjusted for confounders, such as intraocular pressure, keratometric power, height, and antihypertensive drug use, our study excluded participants with ocular pathology and contact lens wear, enabling a more direct assessment of refractive error effects. Aketa et al. [8] reported a sex-specific association, which was not assessed in our cohort. Importantly, our findings demonstrated a consistent trend for a reduced ECD, decreased HEX, and thinner CCT with increasing myopia severity, reinforcing the hypothesis that the biomechanical stress caused by axial elongation compromises endothelial morphology. Taken together, both studies [8] underscore the impact of high myopia on corneal endothelial health, although population-specific and methodological differences highlight the need for further cross-cultural, age-stratified analyses to clarify these associations.

This study provided valuable insights into corneal endothelial morphology alterations across different myopia severities, highlighting significant variations in ECD, HEX, and CCT. A key strength of the study is the population-specific analysis, which offers relevant data for clinical applications. However, study limitations include the cross-sectional study design, which prevents assessment of longitudinal changes, and the exclusion of contact lens wearers, which limits the broader applicability of the results. Future studies should explore long-term endothelial alterations in individuals with high myopia, incorporate diverse populations, and evaluate additional biomechanical factors that influence endothelial health. Such research may enhance clinical strategies for managing myopia-related corneal changes.

CONCLUSIONS

This study highlighted significant alterations in corneal endothelial morphology across varying degrees of myopia. High myopia was associated with a lower ECD, reduced HEX, and thinner CCT, suggesting potential effects of biomechanical stress on corneal endothelial health. These findings provide important insights into the ocular implications of myopia severity, emphasizing the need for continued research on endothelial stability in highly myopic eyes. Understanding these changes may help to refine clinical management strategies and to improve long-term ocular health outcomes in individuals with myopia.

ETHICAL DECLARATIONS

Ethical approval: The study was approved by the IIUM Research Ethics Committee and was conducted in accordance with the tenets of the Declaration of Helsinki. All participants were thoroughly briefed on the procedures, and written informed consent was obtained prior to data collection.

Conflict of interests: None.

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