



<https://doi.org/10.21516/2072-0076-2026-19-2-36-42>

Corneal endothelial cells change in different stages of keratoconus

Rabia Sharif Bhatti, Shama Khan, Hassan Mansoor, Aunaza Maqbool, Rabeeah Zafar, Rabia Faheem✉

Pakistan Institute of Ophthalmology, Al-Shifa Trust Eye Hospital, Rawalpindi, 4600, Pakistan
rabiafaheem3@gmail.com

Purpose. To evaluate the changes in morphology and total endothelial count in patients with different stages of keratoconus (KC). **Material and methods.** A cross-sectional study included 564 eyes of KC patients (57.8% males and 42.2% females) aged 19.9 ± 6.5 years. Study was conducted at the Cornea and Refractive Surgery department of Alshifa trust eye hospital Rawalpindi. Galilei (G4) Dual Scheimpflug Analyzer and specular microscopy (Tomey EM-4000) were used for all eyes examination. KC eyes were classified according to Amsler classification into stage 1, 2, 3 and 4. **Results.** There was statistically significant difference in endothelial cell density ($p < 0.001$) and coefficient of variation ($p = 0.001$) between different stages of KC eyes. Regarding cell surface area and cell morphology, there was statistically significant difference between different stages of KC eyes ($p < 0.001$). **Conclusions.** Significant changes were seen in endothelial cell count and morphology of eyes by using specular microscopy. For stages 1 and 2 KC, these changes are mild but the endothelium in stage 3 and 4 shows significant changes regarding polymegathism and pleomorphism.

Keywords: keratoconus; endothelial cell density; specular microscopy; polymegathism; pleomorphism

Conflicts of interests: there is no conflict of interests.

Financial interest: no author has a financial or property interest in any material or method mentioned.

Acknowledgements. Authors like to express their gratitude for the general support and encouragement they received during the preparation of this article. While no specific contributions were made from any organization for this study.

For citation: Bhatti R.S., Khan S., Mansoor H., Maqbool A., Zafar R., Faheem R. Corneal endothelial cells change in different stages of keratoconus. Russian ophthalmological journal. 2026; 19 (2): 36-42. <https://doi.org/10.21516/2072-0076-2026-19-2-36-42>

Изменения клеток эндотелия роговицы на разных стадиях кератоконуса

Рабия Шариф Бхатти, Шама Хан, Хассан Мансур, Ауназа Макбул, Рабия Зафар, Рабия Фахим✉

Пакистанский институт офтальмологии, офтальмологическая больница «Аль-Шифа», Равалпинди, 4600, Пакистан

Цель работы — оценить изменения морфологии и общего количества эндотелиальных клеток у пациентов с кератоконусом (КК) на разных стадиях заболевания. **Материал и методы.** В поперечное исследование включены 564 глаза пациентов с КК, в том числе 57,8% мужчин и 42,2% женщин, в возрасте $19,9 \pm 6,5$ года. Исследование проводилось в отделении хирургии роговицы и рефракционной хирургии офтальмологической больницы Alshifa Trust в Равалпинди. Всем пациентам выполнено обследование с использованием Galilei (G4) Dual Scheimpflug Analyzer и эндотелиальная микроскопия (Tomey EM-4000). Стадии КК (1, 2, 3 и 4) были определены в соответствии с классификацией Амслера. **Результаты.** Выявлена статистически значимая разница в плотности эндотелиальных клеток ($p < 0,001$) и коэффициенте вариации ($p = 0,001$) между разными стадиями КК. Статистически значимая разница между стадиями КК наблюдалась также по показателю площади клеточной поверхности и по морфологии клеток ($p < 0,001$). **Заключение.** В глазах с КК с помощью эндотелиальной микроскопии выявлены значительные изменения в количестве и морфологии эндотелиальных клеток. На 1-й и 2-й стадиях КК эти изменения незначительны, но на 3-й и 4-й стадиях эндотелий демонстрирует значительные изменения, касающиеся полимегатизма и плеоморфизма.

Ключевые слова: кератоконус; клетки эндотелия; эндотелиальная микроскопия; полимегатизм и плеоморфизм

Конфликт интересов: отсутствует.

Прозрачность финансовой деятельности: никто из авторов не имеет финансовой заинтересованности в представленных материалах или методах.

Благодарности: авторы хотели бы выразить благодарность за общую поддержку и ободрение, оказанные им в процессе подготовки этой статьи. При этом ни одна конкретная организация не внесла вклад в это исследование.

Для цитирования: Бхатти Р.Ш., Хан Ш., Мансур Х., Макбул А., Зафар Р., Фахим Р. Изменения клеток эндотелия роговицы на разных стадиях кератоконуса. Российский офтальмологический журнал. 2026; 19 (2): 36-42. <https://doi.org/10.21516/2072-0076-2026-19-2-36-42>

Keratoconus (KC) is a progressive, bilateral, non-inflammatory, and asymmetrical corneal ectatic disorder characterized by localized stromal thinning and protrusion of the cornea, resulting in irregular astigmatism, myopia, and visual impairment of varying severity [1]. The disease usually begins during adolescence or early adulthood and may continue to progress until the third or fourth decade of life, often leading to significant deterioration in quality of vision and daily functioning. Clinically, patients commonly present with blurred vision, glare, photophobia, monocular diplopia, and frequent changes in refractive correction [2]. Advanced stages of the disease may result in corneal scarring and severe visual disability requiring corneal transplantation.

Recent epidemiological studies suggest that KC is more prevalent than previously recognized, particularly in Asian and Middle Eastern populations [3]. A global systematic review and meta-analysis reported substantial geographic variability in the prevalence and incidence of KC, with South Asian populations demonstrating some of the highest disease burdens worldwide [4]. The prevalence of KC has been reported to range from 0.2 to 4790 cases per 100,000 individuals, while incidence estimates vary between 1.5 and 25 cases per 100,000 individuals annually [4]. Such wide variability may be attributed to differences in diagnostic criteria, corneal imaging modalities, environmental influences, ethnicity, and study methodologies. The higher prevalence observed in South Asian populations has been associated with genetic predisposition, consanguinity, chronic eye rubbing, ultraviolet light exposure, and allergic ocular diseases [5].

Although KC has traditionally been described as a degenerative corneal disorder, increasing evidence suggests that inflammatory, biochemical, and genetic mechanisms also contribute significantly to its pathogenesis [6]. Histopathological studies have demonstrated disruption of stromal collagen lamellae, apoptosis of keratocytes, oxidative stress, and degradation of extracellular matrix components within the cornea [7]. Furthermore, advances in proteomics and molecular biology have revealed abnormalities in both the tear film and corneal epithelium of KC patients. Increased concentrations of degradative enzymes, including matrix metalloproteinases, cathepsins, phosphatases, and lipases, have been identified in the tear film, promoting stromal weakening and corneal remodeling [6]. Altered epithelial proliferation, impaired differentiation, inflammatory cytokine expression, and epithelial–mesenchymal transition have also been implicated in disease progression [8].

The corneal endothelium is a single layer of hexagonal cells located on the posterior surface of the cornea and plays a critical role in maintaining corneal transparency through regulation of stromal hydration. Endothelial cells possess limited regenerative capacity; therefore, morphological or functional alterations may have important implications for corneal health and surgical outcomes [9]. In normal corneas, endothelial morphology is assessed using parameters such as endothelial cell density (ECD), coefficient of variation (CV), and percentage of hexagonal

cells (HEX) through specular microscopy. Polymegathism and pleomorphism are considered indicators of endothelial stress and dysfunction.

Early studies investigating endothelial changes in KC primarily attributed observed pleomorphism and polymegathism to prolonged use of rigid contact lenses rather than the disease itself [10]. However, more recent evidence suggests that KC may intrinsically affect endothelial morphology. Several investigators have reported reduced endothelial cell density, increased coefficient of variation, and decreased hexagonality in moderate and advanced KC eyes compared to healthy controls [11, 12]. M. El-Agha et al. [11] demonstrated significant endothelial morphological abnormalities in KC patients, particularly in advanced stages of the disease. Similarly, A. Elmassry et al. [12] reported alterations in endothelial cell morphology associated with increasing severity of KC, indicating that endothelial involvement may represent part of the disease spectrum rather than merely a secondary effect of contact lens wear. Nonetheless, many previous studies were limited by small sample sizes, retrospective designs, or exclusion of severe grade 4 KC cases.

Evaluation of corneal endothelial morphology in KC is clinically important because endothelial integrity directly influences disease management and surgical planning. In early disease, endothelial assessment may help monitor the long-term effects of rigid gas-permeable or scleral contact lens wear. In advanced KC requiring surgical intervention, endothelial status plays a crucial role in determining the suitability of deep anterior lamellar keratoplasty (DALK) versus penetrating keratoplasty (PK) [13]. Preservation of healthy endothelial cells is associated with improved graft survival and reduced postoperative complications. Therefore, a better understanding of endothelial alterations in KC may contribute to improved patient selection, surgical outcomes, and long-term visual rehabilitation.

Despite the high prevalence of KC in South Asian populations and the increased prevalence of associated risk factors such as atopy, eye rubbing, and consanguinity, limited regional data are available regarding corneal endothelial morphology in KC patients. Most available studies have been conducted in Middle Eastern or European populations, limiting the generalizability of their findings to South Asian individuals. Ethnic and environmental variations may influence disease characteristics and endothelial changes, highlighting the need for population-specific research.

Therefore, the present study aims to evaluate corneal endothelial morphology across different severity grades of keratoconus in a South Asian population using specular microscopy. Assessing endothelial parameters in relation to disease severity may enhance understanding of the pathophysiology of KC and provide valuable information for optimizing clinical management and surgical decision-making.

MATERIAL AND METHODS

The study was conducted as a cross-sectional study in the Department of Cornea and Refractive Surgery at

Table 1. Characteristic of keratoconus stages according to the Amsler — Krumeich classification [14]
Таблица 1. Характеристика стадий кератоконуса согласно классификации Amsler — Krumeich [14]

Stages of KC Стадия КК	Stage 1 Стадия 1	Stage 2 Стадия 2	Stage 3 Стадия 3	Stage 4 Стадия 4
Amsler — Krumeich classification Классификация Amsler — Krumeich	Eccentric corneal steepening Induced myopia and/or astigmatism < 5.00 D Average keratometric value < 48 D Эксцентрическое увеличение кривизны роговицы, миопия и/или астигматизм < 5.00 D, среднее значение кератометрии < 48 D	Induced myopia and/or astigmatism > 5.00 D but < 8.00 D Average keratometric value < 53 D No central scars Minimum apical corneal thickness > 400 µm Миопия и/или астигматизм > 5.00 D, но < 8.00 D, среднее значение кератометрии < 53 D, нет центральных рубцов, минимальная апикальная толщина роговицы > 400 мкм	Induced myopia and/or astigmatism > 8.00 D but < 10.00 D Average keratometric value > 53 D No central scars Minimum apical corneal thickness between 300–400 µm Миопия и/или астигматизм > 8.00 D, но < 10.00 D, среднее значение кератометрии > 53 D, нет центральных рубцов, минимальная апикальная толщина роговицы 300–400 мкм	Refraction not measurable Average keratometric value > 55 D Central scars Minimum apical corneal thickness < 300 µm Рефракция не определяется, среднее значение кератометрии > 55 D, рубцы в центре, минимальная апикальная толщина роговицы < 300 мкм
Polymegathism Полимегатизм	0–200 µm ² , 201–300 µm ² , 301–400 µm ² , 401–500 µm ² , 501–600 µm ² , > 600 µm ²			
Pleomorphism Плеоморфизм	Endothelial cells varying from three-sided (trigonal) to nine-sided (nonagonal) Клетки эндотелия от трехгранной (треугольной) до девятигранной (неагональной) формы			

Al-Shifa Trust Eye Hospital, Rawalpindi, which provides advanced diagnostic and therapeutic services for conditions affecting the anterior surface of the eye. Ethical approval for the study was obtained from the Ethical Review Board of Al-Shifa Trust Eye Hospital, and all procedures were conducted in compliance with the Declaration of Helsinki.

A total of 564 eyes from patients with KC were included in the study. The mean age of the participants was 19.9 ± 6.5 years (range: 8–35 years), and 57.8% (n = 326) were male. Patients were classified according to the Amsler — Krumeich classification system into stages 1, 2 and 3, while stage 4 KC characterized by significant central corneal scarring [14], was excluded from the study.

The study focused on patients with unilateral or bilateral KC. Inclusion criteria for the study were: patients with unilateral or bilateral KC classified into stages 1, 2, or 3 according to the Amsler — Krumeich classification [14]. Exclusion criteria were: age of 35 years, a history of contact lens use, previous ocular surgeries, acute hydrops, previous collagen crosslinking, and form fruste KC.

All patients underwent a complete ophthalmic examination, including both objective and subjective refraction, slit-lamp examination, and detailed fundus evaluation. In cases where indicated, a trial of hard contact lenses was performed. To ensure consistency, a single examiner performed the slit-lamp examination, assessing corneal clarity and the presence of scars. Topographic measurements were obtained using the Galilei (G4) Dual Scheimpflug Analyzer, which provided data on mean keratometric values and apical corneal thickness. Endothelial morphology was assessed with the EM-4000 specular microscope, which provided automatic capture and measurement at an optical magnification of 190 µm. The study variables were derived from specular microscopy reports and included the following: endothelial cell density (ECD), defined as the number of cells per mm² of the cornea; coefficient of variation (CV), calculated by dividing the standard deviation of endothelial cell density by the total dimensions of the analyzed area; polymegathism, which refers to variations in the size and arrangement of endothelial cell

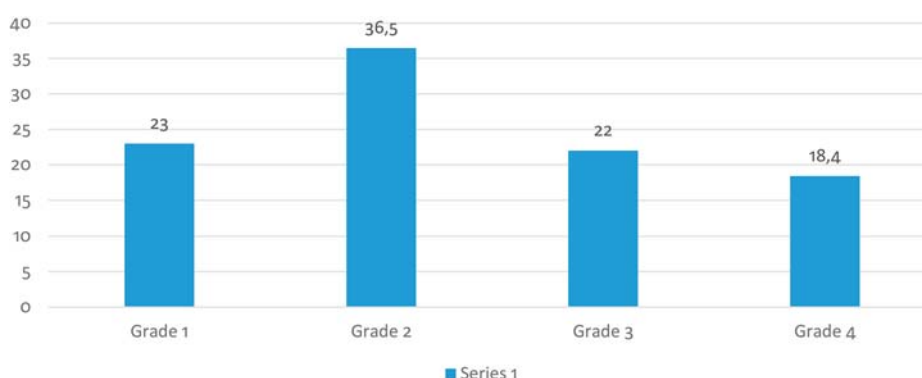


Figure. Distribution of eyes based on severity of keratoconus

Рисунок. Распределение глаз в зависимости от степени тяжести (стадии) кератоконуса

dimensions, categorized into six groups based on cell size, and pleomorphism, which describes changes in the distribution and shape of endothelial cells (Table 1).

The data were stored and analyzed using the Statistical Software for Social Sciences (SPSS) version 22. Descriptive statistics, including arithmetic mean, standard deviation, and range, were calculated for quantitative variables, while frequencies and percentages were used for categorical variables. The normality of the data was assessed using both graphical and statistical methods, with the Kolmogorov — Smirnov test employed for sample sizes greater than 50. For inferential analysis, one-way Analysis of Variance (ANOVA) was used to compare the outcome variables across different stages of KC. If the data did not meet the assumption of normality, the Kruskal — Wallis test was applied instead. Bonferroni adjustments were made for multiple comparisons, and all statistical tests were interpreted at a 95% confidence level.

RESULTS

The best corrected visual acuity (BCVA) and the spherical equivalent had a mean value of 0.4 ± 0.3 (Range = 0.0–1.2) and -5.3 ± -4.1 (Range = 0.0– -22.5) respectively. Based on the Amsler's classification of keratoconus, most eyes belonged to Grade 2 (36.5%, n = 206) while least were present in Grade 4 (18.4%, n = 104) (Figure).

The mean ECD (cells/mm²) was 2620.3 ± 317.3 ranging from 1712/mm² to 3266/mm². The KW test showed a statistically

significant difference between different grades of KC with respect to ECD (χ^2 (df) = 106.3(3), p-value = < 0.001). The average ECD was 2765.2 ± 279.8 and 2335.8 ± 332.2 in Grade 1 and Grade 4 respectively. Moreover, statistically significant difference was also observed in KW test for coefficient of variance (χ^2 (df) = 425.2(3), p-value = < 0.001). The results of Post hoc tests for ECD and CV are provided in detail in Table 2.

Intergroup post hoc comparisons revealed that the highest average percentage of cells within the size range of 301–400 μm^2 was observed in Grade 1 cases (33.7 ± 8.5), while the lowest percentage for this range occurred in Grade 4 cases (26.5 ± 8.5). For the size range of 401–500 μm^2 , Grades 1 (21.3 ± 7.0) and 2 (21.2 ± 6.7) exhibited relatively similar percentages. Regarding the size range of 501–600 μm^2 , Grade 4 displayed the highest mean (14.7 ± 6.6), whereas Grade 3 showed the lowest (9.1 ± 4.4). Detailed post hoc results from the Kruskal — Wallis test are provided in Table 3.

Hexagonal geometry was the most prevalent cell shape, with an overall mean percentage of 41.3 ± 22.1 across all stages of keratoconus. Grade 2 keratoconus exhibited the highest percentage of hexagonal cells (48.1 ± 18.9), while grade 3 showed the lowest (36.1 ± 20.8). In contrast, decagonal cells were the least abundant, with a mean percentage of 0.8 ± 1.8 (range: 0–8). The greatest prevalence of decagonal cells was observed in grade 4 keratoconus (2.0 ± 3.1), followed by grade 3 (1.1 ± 1.8), whereas grades 2 and 1 both had a mean percentage of 0.4. Additional details are presented in Table 4.

DISCUSSION

In KC, early visual impairment is commonly managed with spectacles or rigid gas-permeable contact lenses, which provide satisfactory visual rehabilitation in mild disease. In selected patients, intracorneal ring segments may be used to reduce corneal irregularity and improve visual acuity by flattening

the corneal cone and decreasing astigmatism [15]. As the disease progresses, surgical intervention becomes necessary. Among keratoplasty techniques, deep anterior lamellar keratoplasty (DALK) is increasingly favored over penetrating keratoplasty (PKP) because it preserves the host endothelium, thereby significantly reducing the risk of immunological rejection and endothelial failure [16]. Nevertheless, penetrating keratoplasty remains an important option in advanced KC cases where stromal scarring or severe ectasia compromises visual rehabilitation.

In the present study, corneal endothelial parameters including endothelial cell density (ECD), coefficient of variation (CV), polymegathism, and pleomorphism were evaluated across different stages of KC in 564 eyes classified by severity. Although KC primarily affects the anterior corneal stroma, posterior corneal and endothelial involvement has also been reported in advanced disease [17].

Several mechanisms have been proposed for endothelial alterations in KC, including microtrauma to Descemet's membrane, oxidative stress, ultraviolet radiation exposure, chronic eye rubbing, and long-term contact lens wear [18].

In our study, ECD showed significant variation across KC stages. Previous studies have reported conflicting results. R. Niederer et al. [19] and J. Hollingsworth et al. [20] found no significant difference in ECD between KC stages, suggesting minimal endothelial involvement. In contrast, A. Elmassry et al. [21] and Ö. Uçakhan et al. [22] demonstrated a significant reduction in ECD in advanced KC, indicating progressive endothelial compromise. These discrepancies may be attributed to differences in ethnicity, sample size, imaging modality, and disease grading systems.

Similarly, CV increased with disease severity in our study, indicating progressive endothelial stress. While some studies reported no significant change in CV across KC groups [19],

Table 2. Endothelial Cell Density (ECD) and Coefficient of Variation (CV) Across Different Grades of Keratoconus

Таблица 2. Плотность эндотелиальных клеток (ПЭК) и коэффициент вариации (КВ) при различных стадиях кератоконуса

Grade Стадия	ECD, cells/mm ² ПЭК, кл/мм ²	Range, cells/mm ² Диапазон, кл/мм ²	Mean $\pm$ SD cells/mm ² кл/мм ²	CV КВ	Range CV Диапазон КВ	Mean $\pm$ SD CV КВ	Post Hoc Test Пост хок тест p-value
1	2765.2 ± 279.8	2193–3266	2765.2 ± 279.8	29.7 ± 2.2	20–38	29.7 ± 2.2	$p_1 = 0.07$ $p_2 = 0.005$ $p_3 < 0.001$ $p_4 = 1.00$ $p_5 < 0.001$ $p_6 < 0.001$
2	2668.6 ± 277.0	1822–3108	2668.6 ± 277.0	33.0 ± 2.3	21–52	33.0 ± 2.3	$p_1 < 0.001$ $p_2 < 0.001$ $p_3 < 0.001$ $p_4 < 0.001$ $p_5 < 0.001$ $p_6 < 0.001$
3	2626.9 ± 253.0	1878–2993	2626.9 ± 253.0	36.2 ± 3.0	24–54	36.2 ± 3.0	$p_1 < 0.001$ $p_2 < 0.001$ $p_3 < 0.001$ $p_4 < 0.001$ $p_5 < 0.001$ $p_6 < 0.001$
4	2335.8 ± 332.1	1712–2918	2335.8 ± 332.1	40.6 ± 3.0	25–52	40.6 ± 3.0	$p_1 < 0.001$ $p_2 < 0.001$ $p_3 < 0.001$ $p_4 < 0.001$ $p_5 < 0.001$ $p_6 < 0.001$

Note. SD — Standard Deviation.

Примечание. SD — стандартное отклонение.

Table 3. Polymegathism Across Different Grades of Keratoconus
Таблица 3. Полимегатизм при различных стадиях кератоконуса

Size Range, μm^2 Размер, $\mu\text{м}^2$	Grade 1 Стадия 1 Mean $\pm$ SD	Grade 2 Стадия 2 Mean $\pm$ SD	Grade 3 Стадия 3 Mean $\pm$ SD	Grade 4 Стадия 3 Mean $\pm$ SD	Range Диапазон	Post Hoc Test Пост хок тест p-value
0–200	6.7 $\pm$ 2.1	8.9 $\pm$ 7.9	11.0 $\pm$ 9.0	7.5 $\pm$ 5.9	3–13, 0–37, 2–38, 1–30	$p_1 = 1.00$ $p_2 = 1.00$ $p_3 < 0.001$ $p_4 = 1.00$ $p_5 < 0.001$ $p_6 < 0.001$
201–300	23.7 $\pm$ 9.4	23.3 $\pm$ 8.8	23.4 $\pm$ 7.1	15.7 $\pm$ 8.6	2–35, 2–40, 10–34, 6–36	$p_1 = 1.00$ $p_2 = 1.00$ $p_3 < 0.001$ $p_4 = 1.00$ $p_5 < 0.001$ $p_6 < 0.001$
301–400	33.7 $\pm$ 8.5	28.4 $\pm$ 8.0	30.3 $\pm$ 6.1	26.5 $\pm$ 8.5	23–54, 15–48, 13–39, 14–48	$p_1 < 0.001$ $p_2 = 0.56$ $p_3 < 0.001$ $p_4 = 0.01$ $p_5 < 0.001$ $p_6 < 0.001$
401–500	21.3 $\pm$ 6.9	21.2 $\pm$ 6.7	19.1 $\pm$ 6.9	22.1 $\pm$ 4.4	7–31, 7–32, 3–30, 12–28	$p_1 = 1.00$ $p_2 = 0.02$ $p_3 = 1.00$ $p_4 = 0.04$ $p_5 = 1.00$ $p_6 = 0.005$
501–600	9.7 $\pm$ 5.2	11.2 $\pm$ 6.9	9.1 $\pm$ 4.4	14.7 $\pm$ 6.6	1–16, 1–28, 1–23, 5–25	$p_1 = 1.00$ $p_2 = 0.89$ $p_3 < 0.001$ $p_4 = 0.06$ $p_5 < 0.001$ $p_6 < 0.001$
> 600	0.3 $\pm$ 0.6	1.6 $\pm$ 2.7	3.4 $\pm$ 4.5	8.8 $\pm$ 7.1	0–2, 0–11, 0–24, 0–25	$p_1 = 0.001$ $p_2 < 0.001$ $p_3 < 0.001$ $p_4 < 0.001$ $p_5 < 0.001$ $p_6 < 0.001$

others demonstrated increased variability in advanced disease [21], supporting our findings.

Regarding polymegathism, earlier studies suggested minimal endothelial cell size variation in KC [23] A. However, our staged analysis demonstrated increasing polymegathism with disease severity, suggesting progressive morphological stress on the endothelium.

Pleomorphism analysis showed a significant reduction in hexagonal cells with increasing KC severity. A healthy corneal endothelium typically maintains approximately 60% hexagonal cells, and reduction reflects endothelial dysfunction. Similar findings have been reported by A. Elmassry et al. [21], Ö. Uçakhan et al. [22], and M. Matsuda et al. [23], who demonstrated decreased hexagonality in KC eyes compared to controls.

R. Laing et al. [24] also reported morphological endothelial changes in KC, although earlier literature suggested these findings could be secondary to contact lens wear rather than intrinsic disease pathology.

The variability in published findings may be due to differences in imaging modalities, KC severity distribution, and lack of standardized classification systems across studies.

This study has limitations, including its cross-sectional design, absence of healthy controls, and potential measurement variability inherent to specular microscopy. Additionally, confounding factors such as contact lens wear and eye rubbing were not controlled.

CONCLUSION

In conclusion, our study highlights the progressive changes in corneal endothelial cells across different stages of KC, with more pronounced alterations in advanced stages. These findings underscore the importance of specular microscopy in assessing corneal endothelium before making decisions regarding transplant options. Given the marked endothelial cell changes observed in stages 3 and potentially stage 4 (though not studied here), a full-thickness transplant may be more suitable for advanced KC cases, as it ensures a healthy endothelium for long-term clarity. However, additional research with longitudinal follow-up, inclusion of stage 4 patients, consideration of systemic factors, and healthy controls is essential to further solidify these recommendations and refine treatment strategies

References/Литература

1. Singh RB, Koh S, Sharma N, et al. Keratoconus. *Nat Rev Dis Primers*. 2024; 10: 81. doi: 10.1038/s41572-024-00565-3

2. Rabinowitz YS. Keratoconus. *Surv Ophthalmol*. 1998; 42 (4): 297–319. doi: 10.1016/S0039-6257(97)00119-7

3. Hashemi H, Heydarian S, Hooshmand E, et al. The prevalence and risk factors for keratoconus: a systematic review and meta-analysis. *Cornea*. 2020; 39 (2): 263–70. doi: 10.1097/ICO.0000000000002150

4. Sriranganathan A, Chan CC, Dhillon J, Felfeli T. Global incidence and prevalence of keratoconus: a systematic review and meta-analysis. *Cornea*. 2025. doi: 10.1097/ICO.0000000000003973

Table 4. Comparison of Cell Geometries Across Different Grades of Keratoconus (Polymorphism)
Таблица 4. Сравнение геометрии клеток при различных стадиях кератоконуса (полиморфизм)

Cell Geometry Форма клеток	Grade 1 Стадия 1 Mean $\pm$ SD	Grade 2 Стадия 2 Mean $\pm$ SD	Grade 3 Стадия 3 Mean $\pm$ SD	Grade 4 Стадия 4 Mean $\pm$ SD	Range All Grades Диапазон	p-values
Trigonal Треугольная	0.6 $\pm$ 3.6	0.1 $\pm$ 0.4	0.9 $\pm$ 1.7	3.6 $\pm$ 6.9	0–24	$p_1 = 0.85$ $p_2 < 0.001$ $p_3 < 0.001$ $p_4 < 0.001$ $p_5 = 0.001$ $p_6 = 1.00$
Tetragonal Четырехугольная	2.8 $\pm$ 8.5	3.9 $\pm$ 5.6	9.4 $\pm$ 11.9	7.7 $\pm$ 12.1	0–56	$p_1 < 0.001$ $p_2 < 0.001$ $p_3 < 0.001$ $p_4 = 1.00$ $p_5 = 0.20$ $p_6 = 1.00$
Pentagonal Пятиугольная	13.7 $\pm$ 10.4	21.0 $\pm$ 10.8	24.9 $\pm$ 14.4	16.4 $\pm$ 10.3	0–57	$p_1 < 0.001$ $p_2 < 0.001$ $p_3 = 0.41$ $p_4 = 0.08$ $p_5 = 0.09$ $p_6 < 0.001$
Hexagonal Шестиугольная	38.1 $\pm$ 24.3	48.1 $\pm$ 18.9	36.1 $\pm$ 20.8	38.1 $\pm$ 23.4	0–76	$p_1 = 0.003$ $p_2 = 1.00$ $p_3 = 1.00$ $p_4 < 0.001$ $p_5 = 0.006$ $p_6 = 1.00$
Heptagonal Семиугольная	26.5 $\pm$ 15.9	18.7 $\pm$ 8.3	16.7 $\pm$ 12.8	18.4 $\pm$ 6.4	0–68	$p_1 < 0.001$ $p_2 < 0.001$ $p_3 = 0.004$ $p_4 = 0.77$ $p_5 = 1.00$ $p_6 = 0.13$
Octagonal Восьмиугольная	13.1 $\pm$ 17.1	6.6 $\pm$ 11.0	9.8 $\pm$ 13.1	11.4 $\pm$ 14.0	0–54	$p_1 = 0.001$ $p_2 = 1.00$ $p_3 = 1.00$ $p_4 = 0.008$ $p_5 < 0.001$ $p_6 = 1.00$
Nonagonal Девятиугольная	4.4 $\pm$ 7.0	1.5 $\pm$ 3.8	2.9 $\pm$ 5.1	6.4 $\pm$ 7.8	0–20	$p_1 = 0.05$ $p_2 = 1.00$ $p_3 = 0.007$ $p_4 = 0.04$ $p_5 < 0.001$ $p_6 = 0.01$
Decagonal Десятиугольная	0.4 $\pm$ 0.7	0.4 $\pm$ 0.8	1.1 $\pm$ 1.8	2.0 $\pm$ 3.0	0–8	$p_1 = 1.00$ $p_2 = 0.04$ $p_3 < 0.001$ $p_4 = 0.001$ $p_5 < 0.001$ $p_6 = 0.47$

- Gomes JA, Tan D, Rapuano CJ, et al. Global consensus on keratoconus and ectatic diseases. *Cornea*. 2015; 34 (4): 359–69. doi: 10.1097/ICO.0000000000000408
- Niazi S, Gatzoufas Z, Doroodgar F, et al. Keratoconus: exploring fundamentals and future perspectives — a comprehensive systematic review. *Ther Adv Ophthalmol*. 2024; 16. doi: 10.1177/25158414241232258
- Mathew JH, Goosey JD, Bergmanson JP. Quantified histopathology of the keratoconic cornea. *Optom Vis Sci*. 2011; 88 (8): 988–97. doi: 10.1097/OPX.0b013e31821f9f1f
- Galvis V, Sherwin T, Tello A, et al. Keratoconus: an inflammatory disorder? *Eye*. 2015; 29 (7): 843–59. doi: 10.1038/eye.2015.63
- Bourne WM. Biology of the corneal endothelium in health and disease. *Eye*. 2003; 17 (8): 912–8. doi: 10.1038/sj.eye.6700559
- Laule A, Cable MK, Hoffman CE, Hanna C. Endothelial cell population changes of keratoconus patients. *Am J Optom Physiol Opt*. 1978; 55 (7): 447–54. doi: 10.1097/00006324-197807000-00001
- El-Agha MS, El Sayed YM, Harhara RM. Corneal endothelial changes in keratoconus patients. *Benha Med J*. 2022; 39 (3): 1–8. doi: 10.21608/bmj.2022.250760
- Elmassry A, Said DG, Dua HS. Evaluation of corneal endothelial cell changes in keratoconus. *Eye Contact Lens*. 2021; 47 (6): 345–50. doi: 10.1097/ICL.0000000000000762
- Reinhart WJ, Musch DC, Jacobs DS, et al. Deep anterior lamellar keratoplasty as an alternative to penetrating keratoplasty: a report by the American Academy of Ophthalmology. *Ophthalmology*. 2011; 118 (1): 209–18. doi: 10.1016/j.ophtha.2010.11.002
- Ento Key. Keratoconus classification systems. Available from: <https://entokey.com/keratoconus-classification-systems/> [cited 2026 May 21].
- Shabayek MH, Alio JL. Intrastromal corneal ring segments for keratoconus: clinical outcomes and visual performance. *J Cataract Refract Surg*. 2007; 33 (7): 1308–14. doi: 10.1016/j.jcrs.2007.03.029
- Borderie VM, Sandali O, Bullet J, et al. Long-term results of deep anterior lamellar keratoplasty versus penetrating keratoplasty. *Ophthalmology*. 2012; 119 (2): 249–55. doi: 10.1016/j.ophtha.2011.07.058
- Jhanji V, Sharma N, Vajpayee RB, et al. Management of keratoconus: current perspective. *Br J Ophthalmol*. 2011; 95 (8): 1044–50. doi: 10.1136/bjo.2010.190090

18. Galvis V, Sherwin T, Tello A, et al. Keratoconus: an inflammatory disorder? *Eye (Lond)*. 2015; 29: 843–59. doi: 10.1038/eye.2015.63
19. Niederer RL, Perumal D, Sherwin T, et al. Keratoconus and endothelial morphology. *Cornea*. 2007; 26 (5): 590–6. doi: 10.1097/ICO.0b013e31803bbdbdc
20. Hollingsworth JG, Bonshek RE, Efron N, et al. Morphology of corneal endothelium in keratoconus. *Eye*. 2005; 19: 1162–6. doi: 10.1038/sj.eye.6701732
21. Elmassry A, Said DG, Dua HS, et al. Corneal endothelial cell changes in keratoconus. *Eye Contact Lens*. 2021; 47 (6): 345–50. doi: 10.1097/ICL.0000000000000762
22. Uçakhan ÖÖ, Özkan M, Kanpolat A, et al. Corneal endothelial changes in keratoconus. *Cornea*. 2006; 25 (6): 708–13. doi: 10.1097/01.ico.0000227880.64302.8d
23. Matsuda M, Suda T, Manabe R, et al. Corneal endothelial changes in keratoconus. *Am J Ophthalmol*. 1982; 93 (3): 342–9. doi: 10.1016/0002-9394(82)90327-6
24. Laing RA, Sandstrom MM, Berrospi AR, et al. Morphological changes in keratoconus endothelium. *Arch Ophthalmol*. 1979; 97 (10): 1865–7. doi: 10.1001/archophth.1979.01020020687011

Author's contributions: Rabia Sahrif Bhatti — conception and design, data acquisition, analysis and interpretation, drafting; Shama Khan, Hassan Mansoor — revising and critical review, analysis and interpretation; Aunaza Maqbool, Rabeeah Zafar — revising and critical review; Rabia Faheem — interpretation, revising and critical review, final approval of the work.

Вклад авторов в работу: Рабия Сахриф Бхатти — разработка концепции и дизайна, сбор данных, анализ и интерпретация, написание текста; Шама Хан, Хассан Мансур — редактирование и критический анализ, анализ и интерпретация; Ауназа Макбул, Рабия Зафар — редактирование и критический анализ; Рабия Фахим — интерпретация, редактирование и критический анализ, окончательное утверждение работы.

Originally received: 15.02.2025. Final revision: 13.07.2025. Accepted: 15.07.2025

Поступила: 15.02.2025. Переработана: 13.07.2025. Принята к печати: 15.07.2025

INFORMATION ABOUT THE AUTHORS/ИНФОРМАЦИЯ ОБ АВТОРАХ

Pakistan Institute of Ophthalmology, Al-Shifa Trust Eye Hospital Rawalpindi, 4600, Pakistan

Sharif Bhatti — Ophthalmic Corneal Surgeon, Department of Cornea and Refractive Surgery

Shama Khan — Ophthalmic Corneal Surgeon, Department of Cornea and Refractive Surgery

Hassan Mansoor — Ophthalmic Corneal Surgeon, Department of Cornea and Refractive Surgery

Aunaza Maqbool — Pediatric ophthalmologist, Department of Pediatric Ophthalmology

Rabeeah Zafar — Pediatric ophthalmologist, Department of Pediatric Ophthalmology

Rabia Faheem — Optometrist

For contacts: Rabia Faheem,
rabiafahim3@gmail.com

Пакистанский институт офтальмологии, глазная больница «Аль-Шифа», Равалпинди, 4600, Пакистан

Шариф Бхатти — офтальмохирург — специалист по роговице, отделение хирургии роговицы и рефракционной хирургии

Шама Хан — офтальмохирург — специалист по роговице, отделение хирургии роговицы и рефракционной хирургии

Хассан Мансур — офтальмохирург — специалист по роговице, отделение хирургии роговицы и рефракционной хирургии

Ауназа Макбул — детский офтальмолог, отделение детской офтальмологии

Рабия Зафар — детский офтальмолог, отделение детской офтальмологии

Рабия Фахим — оптометрист

Для контактов: Rabia Faheem,
rabiafahim3@gmail.com