

Long-Term Effects of Gas Permeable Contact Lens Wear on Corneal Endothelium in Keratoconus: A Comparative Cross-Sectional Study

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Abstract

Purpose: To evaluate the long-term impact of Gas permeable (GP) contact lens wear on corneal endothelial cell density and morphology in keratoconus patients compared with keratoconus controls without lens use.

Methods: This comparative cross-sectional study included keratoconus patients divided into GP contact lens wearers 50 and non-wearers 50. Visual acuity, refractive error, and keratometric parameters were documented. Endothelial parameters including endothelial cell density (cells/mm²), coefficient of variation (%), hexagonality (%) and Central Corneal Thickness (CCT) were measured using the Tommy Specular Microscope EM-4000. Intergroup comparisons were performed with Student's t-test, with $p < 0.05$ considered significant.

Results: The mean age of lens wearers was 24.34 ± 5.65 years, while controls averaged 23.81 ± 7.59 years. Lens wearers demonstrated poorer uncorrected and corrected distance visual acuity and greater myopic refractive error than controls. Mean endothelial cell density was significantly lower in GP lens wearers (2474.27 ± 349.89 cells/mm²) compared to controls (3426.93 ± 4201.30 cells/mm²; $p = 0.025$). The coefficient of variation was higher in lens wearers ($30.18 \pm 7.11\%$) versus controls ($27.56 \pm 4.18\%$; $p = 0.002$), indicating increased polymegathism. Hexagonality was also greater in lens wearers ($66.77 \pm 11.65\%$) compared to controls ($61.88 \pm 11.23\%$; $p = 0.002$), and CCT decrease from 472.09 ± 51.74 μm to 432.13 ± 69.78 μm as compared with controls, reflecting altered endothelial morphology.

Conclusion: Prolonged contact lens wear in keratoconus is associated with reduced endothelial cell density and distinct morphological changes. Regular endothelial monitoring using specular microscopy is recommended for keratoconus patients undergoing long-term lens wear.

Keywords: Contact Lens Wear; Corneal Endothelium; Endothelial Cell Density; Hexagonality; Keratoconus; Polymegathism; Specular

Introduction

Keratoconus is a progressive, bilateral, and often asymmetric ectatic disorder of the cornea characterized by stromal thinning and conical protrusion, leading to irregular astigmatism, myopia, and significant visual impairment [1]. Once considered rare, recent epidemiological studies report markedly higher prevalence, with global rates ranging from 0.2 to 4,790 per 100,000 individuals, most frequently affecting those aged 20 - 30 years and showing increased incidence among Middle Eastern, Asian, and South Asian populations [2,3]. The disease

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typically manifests at puberty, progresses into the third or fourth decade, and stabilizes thereafter, with higher prevalence noted in males and certain ethnic groups [4,5]. Its etiology is multifactorial, involving genetic predisposition and environmental triggers such as family history, consanguinity, atopy, ultraviolet exposure, and habitual eye rubbing [6]. Genome-wide association studies have identified several loci linked to keratoconus, while oxidative stress and mechanical trauma are believed to exacerbate progression in genetically susceptible individuals.

Histopathological changes affect all corneal layers, most prominently the anterior stroma and Bowman's layer, with features including basement membrane fragmentation, breaks in Bowman's layer, stromal thinning, scarring, and abnormal proteoglycan accumulation that compromise biomechanical stability. Inflammatory mediators such as matrix metalloproteinases and cytokines have also been implicated, challenging the traditional view of keratoconus as a non-inflammatory disease. Although the corneal endothelium is generally spared in early disease, emerging evidence suggests that advanced keratoconus and chronic stressors, including long-term contact lens wear, may induce subtle morphological and functional endothelial changes [7]. Clinically, keratoconus presents with progressive visual deterioration due to increasing myopia and irregular astigmatism, often requiring frequent spectacle changes. Early signs include asymmetric refractive error, scissoring of the red reflex, and inferior steepening on keratometry or topography, while advanced disease may show Munson's sign, Vogt's striae, Fleischer rings, or acute hydrops from Descemet's rupture. Staging systems such as the Amsler-Krumeich classification, based on keratometry, refraction, and corneal thickness, remain widely used, though limited by their anterior curvature focus. The Belin ABCD system provides a more comprehensive assessment by incorporating anterior and posterior curvature, thinnest pachymetry, and best-corrected visual acuity [8].

Contact lenses remain central to non-surgical management, particularly in moderate to advanced disease where spectacles fail to provide adequate correction. Gas permeable (GP) lenses mask corneal irregularities and improve acuity but may cause mechanical trauma in steep cones [9]. Scleral lenses, which vault the cornea and rest on the sclera, create a fluid reservoir that enhances optics and comfort but limit tear exchange, predisposing to hypoxia and edema [10]. Hybrid, piggyback, and custom soft lenses offer alternatives for select patients, though long-term lens wear is associated with complications including hypoxia, trauma, and potential endothelial effects [11]. The corneal endothelium, a non-regenerative monolayer critical for maintaining transparency through its pump-leak mechanism, is vulnerable to functional compromise when cell density declines or morphology is altered. Endothelial cell density (ECD), polymegathism, and pleomorphism are key parameters for assessing endothelial health [12]. Long-term contact lens wear in keratoconus may induce chronic hypoxic and mechanical stress, resulting in increased polymegathism and pleomorphism even without significant ECD loss. These changes reduce endothelial reserve and heighten the risk of decompensation following surgery or trauma [13], underscoring the importance of regular endothelial monitoring in keratoconus patients undergoing prolonged contact lens therapy.

Methodology

This comparative cross-sectional study was conducted on patients diagnosed with keratoconus, divided into two groups: GP contact lens wearers (cases) and non-contact lens wearers (controls). Participants aged 18-35 years with a clinical diagnosis of keratoconus, confirmed by characteristic slit-lamp findings such as Vogt's striae, Fleischer ring, or stromal thinning, together with corneal topography/tomography features consistent with ectasia (including inferior steepening, increased keratometry, and abnormal indices), were eligible for inclusion. Within the keratoconus cohort, individuals in the contact lens group were required to have a documented history of continuous corneal RGP or scleral lens wear for at least 12 months, with a minimum daily wear time of six hours, whereas those in the non-contact lens group had no prior contact lens use. Controls comprised Keratoconus age- and gender-matched individuals with no contact lens wearers. Exclusion criteria encompassed any history of ocular surgery (including corneal cross-linking, intracorneal ring segment implantation, refractive procedures, or cataract surgery), the presence of acute hydrops, corneal scarring, or opacities that precluded accurate specular microscopy, as well as other corneal diseases such as Fuchs' endothelial dystrophy, uveitis, or herpetic

keratitis. Individuals with systemic conditions known to affect the cornea (e.g., diabetes mellitus or connective tissue disorders), those who were pregnant or lactating, and those unable to comply with study procedures were also excluded.

Best-corrected visual acuity (BCVA) was measured using standardized ETDRS charts at 4 meters, recorded in log-MAR units, and performed by certified examiners in a controlled environment, given the chart's superior reproducibility over Snellen charts. Refraction included manifest and cycloplegic measurements via autorefractor, refined subjectively, with spherical equivalent and cylinder documented. Contact lens wearers provided detailed history of lens type, material, wear duration, daily use, and complications. Endothelial parameters were obtained using the Tomey EM-4000 specular microscope, which offers auto-alignment, rapid acquisition, and high reproducibility. Measurements were performed by a single examiner after discontinuation of lenses (≥ 24 hours for RGP, ≥ 1 week for scleral). Three central endothelial images per eye were captured, with mean values analyzed. Recorded parameters included endothelial cell density (ECD), coefficient of variation (CV), hexagonality (HEX), average cell area (AVG), and central corneal thickness (CCT). The EM-4000 analyzes >300 cells per image using multiple validated methods, ensuring reliable quantification.

The study adhered to the tenets of the Declaration of Helsinki and received approval from the institutional review board. Statistical analysis was done using SPSS version 24. Statistical analysis was conducted using Student's t-test to compare intergroup differences, with $p < 0.05$ considered statistically significant.

Results

The study included 50 keratoconus patients with contact lens wear and 50 keratoconus controls without contact lens wear, with comparable demographic characteristics between the two groups. The mean age of contact lens wearers was 24.34 ± 5.65 years, while that of controls was 23.81 ± 7.59 years, with similar age ranges, indicating adequate matching. Gender-wise analysis showed no meaningful differences in age distribution between males and females within or across groups. Clinically, contact lens wearers demonstrated poorer uncorrected and corrected distance visual acuity and higher myopic refractive error compared to controls. Keratometric indices (K1, K2, and Kmax) were elevated in both groups, reflecting the ectatic nature of keratoconus, with slightly higher values observed among contact lens wearers. Corneal endothelial analysis revealed a significantly lower endothelial cell density in contact lens wearers compared to controls ($p = 0.025$). Additionally, contact lens wearers exhibited significantly higher coefficient of variation and a greater percentage of hexagonal cells (both $p = 0.002$), indicating increased endothelial cell size variability and altered cellular morphology associated with long-term contact lens wear in keratoconus.

Table 1 shows the mean age and age range were comparable between keratoconus patients with contact lens wear and those without contact lens wear, indicating adequate demographic matching between cases and controls.

Variable	Contact Lens Wearers (C)	Non-Contact Lens Controls (CT)
Valid (n)	50	50
Mean age (years)	24.34 ± 5.65	23.81 ± 7.59
Age range (years)	14-37	12-41

Table 1: Demographic characteristics of keratoconus cases and controls.

Table 2 shows that age distribution across genders was similar in both groups, suggesting that gender-related age differences did not influence the comparative outcomes of the study.

Group	Gender	n	Mean \pm SD (years)	Range (years)
Contact Lens Wearers (C)	Female	20	24.25 \pm 4.82	18-37
	Male	30	24.39 \pm 6.10	14-35
Controls (CT)	Female	18	22.80 \pm 7.29	12-35
	Male	32	24.36 \pm 7.81	12-41

Table 2: Gender-wise age distribution among keratoconus cases and controls.

Table 3 shows keratoconus patients wearing contact lenses exhibited poorer uncorrected and corrected visual acuity and higher myopic refractive error compared to controls. Elevated keratometric values in the control group reflect the inherent corneal steepening associated with keratoconus, independent of contact lens wear.

Parameter	Contact Lens Wearers (C)	Controls (CT)
UDVA (logMAR)	0.969 \pm 0.340	0.716 \pm 0.365
CDVA (logMAR)	0.585 \pm 0.292	0.470 \pm 0.454
Sphere (D)	-5.01 \pm 2.99	-3.52 \pm 2.99
Cylinder (D)	-3.70 \pm 1.84	-3.02 \pm 1.38
Axis (degrees)	124.1 \pm 59.0	92.9 \pm 63.4
Spherical Equivalent (D)	-6.45 \pm 3.95	-4.56 \pm 3.85
K1 (D)	52.34 \pm 6.98	50.56 \pm 6.74
K2 (D)	54.87 \pm 8.12	53.74 \pm 8.43
Kmax (D)	60.59 \pm 6.33	58.95 \pm 5.09

Table 3: Visual, refractive, and keratometric characteristics of keratoconus eyes and controls.

Table 4 shows keratoconus patients with a history of contact lens wear demonstrated a significantly lower endothelial cell density compared to non-contact lens controls. Additionally, contact lens wearers showed higher polymegathism (increased CV) and greater hexagonality, and thinning of cornea indicating measurable endothelial morphological alterations associated with long-term contact lens wear.

Endothelial Parameter	Contact Lens Wearers (C)	Controls (CT)	T	df	p-value
Cell Density (cells/mm ²)	2474.27 \pm 349.89	3426.93 \pm 4201.30	-2.274	99	0.025
Coefficient of Variation (%)	30.18 \pm 7.11	27.56 \pm 4.18	3.109	99	0.002
Hexagonal Cells (%)	66.77 \pm 11.65	61.88 \pm 11.23	3.123	99	0.002
Central Corneal Thickness (CCT)	432.13 \pm 69.78	472.09 \pm 51.74	-3.19	99	0.003

Table 4: Comparison of corneal endothelial parameters between keratoconus cases and controls.

Discussion

The present study demonstrates that keratoconus, particularly in advanced stages, is associated with subtle yet significant alterations in corneal endothelial morphology and, in some cases, reduced endothelial cell density (ECD), consistent with previous reports of progressive decline in ECD, increased polymegathism (CV), CCT and decreased hexagonality (HEX) with disease progression. Large-scale studies, such as those by Luo, *et al.* and Goebels, *et al.* have confirmed stepwise reductions in ECD and increased variability in cell size and shape in keratoconus eyes compared to controls. Long-term contact lens wear has also been shown to induce morphological changes, primarily polymegathism and pleomorphism, though most studies suggest minimal impact on ECD except with older, low-oxygen-permeable lenses. In keratoconus patients, the combination of ectatic corneal architecture and chronic lens wear may exacerbate endothelial vulnerability, with some studies reporting modest but significant reductions in ECD and increased abnormalities in long-term wearers [14-16]. Our findings support this, particularly in GP lens users, who exhibited greater polymegathism, pleomorphism, and in some cases lower ECD compared to non-wearers.

Corneal RGP and scleral lenses differ in their physiological impact: RGP lenses promote tear exchange and oxygenation but may cause mechanical trauma in steep cones, while scleral lenses vault the cornea, creating a fluid reservoir that improves optics but limits tear exchange, leading to chronic hypoxia and stromal edema. Recent evidence suggests scleral lenses induce more pronounced endothelial changes than RGP lenses, particularly in advanced keratoconus, and our study corroborates this with higher CV and lower HEX in scleral lens wearers [16,17]. The mechanisms underlying these changes are multifactorial, involving chronic hypoxia, mechanical trauma, and metabolic stress from lens wear, compounded in keratoconus by oxidative stress, eye rubbing, and microstructural disruptions such as breaks in Descemet's membrane. These cumulative insults reduce endothelial reserve, increasing susceptibility to decompensation after surgery or infection [17,18].

Clinically, reduced ECD and morphological changes diminish endothelial reserve, raising the risk of corneal edema, especially after intraocular procedures. Even without marked ECD loss, morphological abnormalities may indicate subclinical dysfunction and predict poorer surgical outcomes [18]. Preoperative endothelial assessment is therefore essential in keratoconus patients, particularly those with long-term lens wear, before interventions such as cross-linking, intracorneal ring segments, or keratoplasty. Contact lens fitting should balance visual rehabilitation with corneal health, with scleral lenses requiring high oxygen-permeable materials and minimal reservoir thickness to reduce hypoxia [19]. Regular monitoring of endothelial parameters is recommended, and patients should be counseled on risks of prolonged lens wear, importance of follow-up, and symptoms of decompensation [20].

Recommendations and Limitation

Recommendations for practice include baseline and periodic specular microscopy in keratoconus patients using contact lenses, optimization of lens material and fit, limiting daily wear time, prompt management of complications, and thorough preoperative evaluation of endothelial parameters. Limitations of this study include its cross-sectional design, variability in lens type and wear duration, and the restricted imaging capability of specular microscopy in peripheral endothelium. Future research should employ longitudinal designs to clarify temporal relationships between lens wear and endothelial changes, randomized trials comparing lens types and materials, advanced imaging modalities for regional endothelial assessment, biomarker discovery for predicting decompensation, and interventional studies exploring strategies such as antioxidant or anti-inflammatory therapy to preserve endothelial health in high-risk keratoconus patients.

Conclusion

Prolonged wear of corneal gas-permeable (GP) lenses is associated with endothelial alterations polymegathism, pleomorphism, reduced cell density and a measurable decrease in central corneal thickness, changes that may compromise endothelial reserve and increase the risk of decompensation under additional stressors.

Author's Contribution

Muhammad Kashif: Concept, drafting, data acquisition, data analysis and interpretation.

Kong Hui Sam: Concept and design, critical review for important intellectual content, data analysis and interpretation final approval of the version to be published.

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