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Comparison of Corneal Endothelial Parameters in Uveitis and Healthy Eyes Using Specular Microscopy: A Cross-Sectional Study

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Abstract: ***Background***: Corneal endothelial integrity is essential for transparency and surgical prognosis. Anterior uveitis is frequently associated with endothelial alterations, but comparative clinic-based studies using accessible imaging such as specular microscopy are limited. ***Objective***: To evaluate and compare corneal endothelial parameters in eyes with uveitis and healthy controls using non-contact specular microscopy, and to contrast endothelial morphology during active vs inactive inflammation. ***Methods***: Comparative cross-sectional study of 60 eyes (30 uveitis — 15 active, 15 inactive — and 30 age- and sex-matched controls). Non-contact specular microscopy (TOMEY Ver.1F.1U) provided endothelial cell density (ECD), coefficient of variation (CV), hexagonality (HEX %), and central corneal thickness (CCT). Standardized clinical grading (SUN) was used for inflammation. Statistical comparisons employed t tests or Mann–Whitney U tests as appropriate; $p < 0.05$ was significant. ***Results***: Mean ECD was 2246 ± 181 cells/mm² in uveitis eyes vs 2662 ± 154 cells/mm² in controls ($p < 0.001$). Active uveitis: 2168 ± 187; inactive: 2324 ± 165 ($p = 0.003$). CV was higher in uveitis (mean 40.7 ± 5.4%) versus controls (32.1 ± 3.8%; $p < 0.001$). HEX% decreased in uveitis (48.0 ± 5.6%) compared with controls (56.8 ± 5.0%; $p < 0.001$). CCT showed a mild increase in active uveitis (553 ± 24 µm) vs controls (531 ± 20 µm; $p = 0.01$). Keratic precipitates (KPs) correlated with lower ECD ($p = 0.004$). ***Conclusions***: Uveitis is associated with demonstrable endothelial cell loss, increased polymegathism and pleomorphism, and mild CCT changes, with active inflammation showing greater compromise. Specular microscopy provides clinically useful, noninvasive quantification of endothelial health in uveitis and aids surgical planning. The quantitative endothelial metrics generated may also serve as structured imaging data for future bioinformatic and predictive modeling approaches in inflammatory eye disease.

Keywords: Anterior uveitis, Corneal endothelium, Specular microscopy, Endothelial cell density, Corneal endothelial morphology.

BACKGROUND

Corneal endothelial cells form a monolayer whose pump-and-barrier function maintains stromal deturgescence and optical clarity. Because human corneal endothelial cells have very limited proliferative capacity, insults that reduce cell density or disrupt morphology (polymegathism and pleomorphism) may have long-term repercussions for corneal transparency and surgical outcomes.[1–3]

Anterior uveitis is the commonest anatomic form of intraocular inflammation and may occur in isolation or with systemic disease (e.g., HLA-B27 spondyloarthropathies, Behçet disease, sarcoidosis, herpetic disease). Intraocular inflammation exposes the endothelium to inflammatory mediators, immune cells, and keratic precipitates (KPs), any of which may injure endothelial cells directly or induce functional disturbance.[4–6]

Several clinic-based and laboratory studies have indicated endothelial alterations in uveitic eyes, including reduced endothelial cell density (ECD), increased coefficient of variation (CV), reduced percentage hexagonality (HEX%), and, occasionally, increased central corneal thickness (CCT). Pillai et al.

used specular microscopy to document localized endothelial abnormalities adjacent to KPs with partial recovery on resolution of inflammation.[7] Alfawaz et al. (large cross-sectional cohort) and later investigators reported lower ECD and reduced HEX% in uveitic eyes compared with controls.[8,9] Animal models show inflammatory recruitment and endothelial activation in endotoxin-induced uveitis.[10] A recent systematic review and meta-analysis confirms that anterior chamber inflammation is associated with consistent changes in endothelial metrics across multiple studies.[11]

Despite these advances, gaps remain: many prior reports focus on specific uveitis subtypes (e.g., Fuchs', Behçet's, viral uveitis) or use specialized imaging (confocal microscopy) that is not universally available. Clinic-based noncontact specular microscopy provides a practical tool for routine assessment, but comparative data that consider activity status (active vs inactive), the presence of KPs, intraocular pressure (IOP), and systemic associations are relatively limited. This study tests the hypothesis that uveitis (particularly active inflammation) is associated with measurable endothelial cell loss and morphological change compared with healthy eyes, and that these alterations correlate with clinical markers of inflammation.

METHODOLOGY

Study design and setting. Comparative cross-sectional observational study at the Department of Ophthalmology, R. L. Jalappa Hospital and Research Centre, Kolar. Study period: 1 year. Institutional ethics approval and written informed consent were obtained.

Participants. Sample size: 60 (30 uveitis eyes — active or inactive; 30 age- and sex-matched healthy controls). Inclusion criteria: age 15–50 years; Group 1 included patients with anterior, intermediate, or panuveitis presenting with active or inactive disease; Group 2 healthy volunteers without ocular inflammation. Exclusion criteria: prior ocular surgery, ocular trauma, glaucoma, corneal dystrophy (including Fuchs), keratoconus, contact lens wear. Uveitis diagnosis and grading used SUN criteria (AC cells and flare), presence of KPs, iris nodules, synechiae, and presence/absence of hypopyon were recorded.[1]

Clinical evaluation. All participants underwent best-corrected visual acuity, slit-lamp biomicroscopy, dilated fundus exam with +90D lens, and Goldmann applanation tonometry. For uveitis cases, disease duration, laterality, etiologic diagnosis when available (HLA-B27, herpetic, Behçet's, idiopathic), and systemic associations were recorded.

Specular microscopy. A single central image from each eye was captured with a non-contact specular microscope (TOMEY Ver.1F.1U). The device software computed: endothelial cell density (ECD, cells/mm²), coefficient of variation (CV, %), hexagonality percentage (HEX%), minimum/maximum/average cell area, and central corneal thickness (CCT, μm). Images with poor quality or <75 analyzable cells were excluded. Image acquisition and analysis were performed by a single trained operator to reduce interobserver variability.[12–13]

Statistical analysis. Data were entered into Microsoft Excel and analyzed with SPSS v22. Continuous variables are presented as mean ± SD (or median with IQR for non-normal data); categorical variables are frequencies/percentages. Between-group comparisons used Student's t test or Mann–Whitney U test; active vs inactive comparisons used one-way ANOVA with post-hoc tests or Kruskal–Wallis as appropriate. Correlations were assessed with Pearson or Spearman coefficients. A two-tailed $p < 0.05$ was considered statistically significant.

RESULTS

Figure 1. Etiological distribution of uveitis cases included in the study.

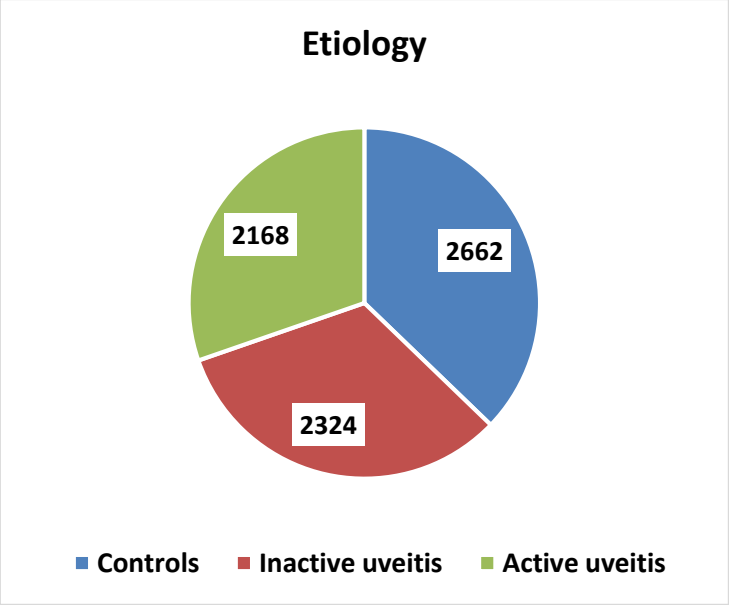

Figure 2. Comparison of mean corneal endothelial cell density (ECD) among control eyes and eyes with inactive and active uveitis.

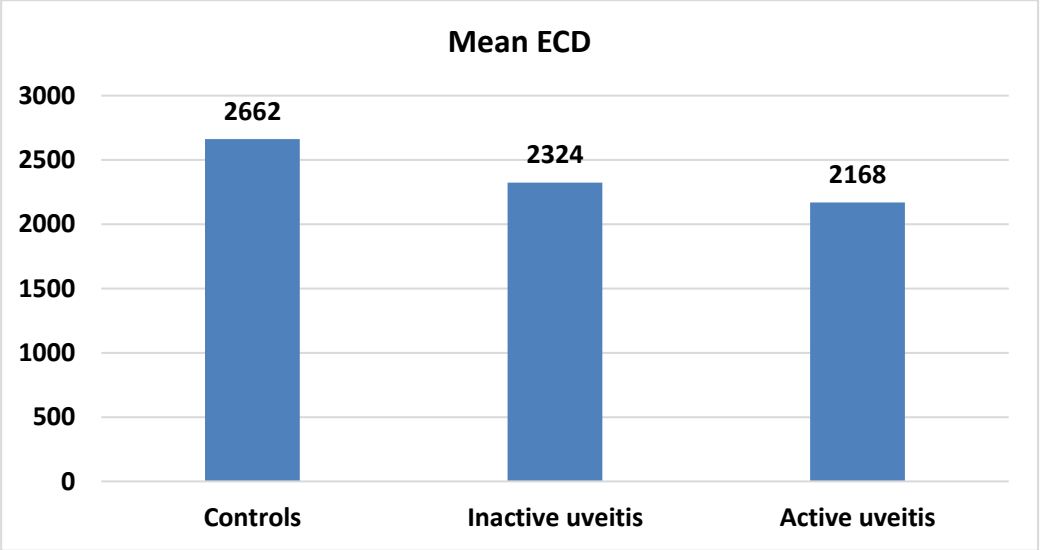

Table 1. Demographic and Clinical Characteristics of Study Participants

Parameter	Uveitis (n = 30)	Controls (n = 30)	p-value
Age (years)	31.4 ± 8.2	30.7 ± 7.9	0.72
Sex (M/F)	18 / 12	17 / 13	0.80
Laterality (R/L)	16 / 14	15 / 15	0.82
Active / Inactive uveitis	15 / 15	—	—
Etiology	Idiopathic 45% HLA-B27 associated 33% Viral/Post-infectious 22%	—	—
Duration of disease (months)	7.8 ± 3.1	—	—

Table 2. Specular Microscopy Parameters in Controls and Uveitis Patients

Parameter	Controls (n = 30)	Uveitis Total (n = 30)	Inactive (n = 15)	Active (n = 15)	p-value (Control vs Uveitis)	p-value (Active vs Inactive)
Endothelial Cell Density	2662 ± 154	2246 ± 181	2324 ± 165	2168 ± 187	<0.001	0.003

(ECD, cells/mm²)						
Coefficient of Variation (CV, %)	32.1 ± 3.8	40.7 ± 5.4	38.6 ± 4.9	42.8 ± 5.7	<0.001	0.01
Hexagonality (HEX, %)	56.8 ± 5.0	48.0 ± 5.6	49.7 ± 4.6	45.3 ± 5.1	<0.001	0.02
Central Corneal Thickness (CCT, µm)	531 ± 20	549 ± 23	545 ± 21	553 ± 24	0.01	0.18
Keratic Precipitates (KPs, %)	—	60% (active only)	—	60%	—	—

Table 3. Endothelial Parameters According to Presence of Keratic Precipitates (KPs)

Parameter	KPs Present (n = 9)	KPs Absent (n = 6)	p-value
Endothelial Cell Density (ECD, cells/mm²)	2120 ± 172	2360 ± 158	0.004
Coefficient of Variation (CV, %)	43.2 ± 5.1	38.7 ± 4.6	0.03
Hexagonality (HEX, %)	45.0 ± 5.0	50.2 ± 4.8	0.02
Central Corneal Thickness (CCT, µm)	552 ± 23	544 ± 21	0.12

Table 3 includes only active uveitis eyes with gradable specular images.

Additional Clinical Associations:

- Duration of inflammation showed a moderate negative correlation with ECD (r = –0.42, p = 0.02).
- Intraocular pressure remained within normal limits across all groups, with no significant differences (p = 0.41).

Participant Characteristics. A total of 60 eyes from 60 participants were included, comprising 30 uveitis eyes and 30 age- and sex-matched healthy controls. The mean age was comparable between uveitis (31.4 ± 8.2 years) and control groups (30.7 ± 7.9 years, p = 0.72), with no significant differences in sex distribution or laterality. Within the uveitis group, 15 eyes had active inflammation and 15 were inactive. Etiologies included idiopathic (45%), HLA-B27-associated (33%), and viral/post-infectious causes (22%).

Corneal Endothelial Parameters. Corneal endothelial metrics were significantly altered in uveitic eyes compared with healthy controls. Endothelial cell density (ECD) was markedly reduced in uveitis eyes, with the lowest values observed in active inflammation. Correspondingly, coefficient of variation (CV) was elevated, indicating increased polymegathism, while hexagonality (HEX%) was decreased, reflecting greater pleomorphism. Central corneal thickness (CCT) showed a mild increase in uveitic eyes, most pronounced in active disease.

Impact of Inflammation Activity. Active uveitis was associated with more pronounced endothelial compromise than inactive disease. Eyes with active inflammation demonstrated lower ECD, higher CV, and reduced HEX% compared with eyes in the inactive phase, highlighting the effect of ongoing inflammation on endothelial integrity.

Associations with Keratic Precipitates and Disease Duration. The presence of keratic precipitates (KPs), observed in 60% of active cases, correlated with lower ECD and higher CV, suggesting localized endothelial injury. Longer duration of inflammation also showed a moderate negative correlation with ECD (r = –0.42, p = 0.02), indicating cumulative endothelial compromise over time.

Intraocular Pressure. Intraocular pressure remained within normal limits across all groups and did not differ significantly between uveitic and control eyes (p = 0.41).

Summary

Overall, uveitic eyes exhibited significant endothelial cell loss, increased polymegathism, decreased hexagonality, and mild corneal thickening, with the most severe changes observed during active inflammation. Endothelial alterations correlated with clinical markers such as KPs and disease duration, underscoring the clinical relevance of monitoring endothelial health in uveitis.

DISCUSSION

This cross-sectional study demonstrates that anterior uveitis is associated with measurable compromise of the corneal endothelium: a significant reduction in central endothelial cell density, greater cell size heterogeneity (increased CV), decreased hexagonality

(reduced HEX%), and a mild increase in central corneal thickness — changes that are amplified during active inflammation. These findings align closely with previously published clinic-based studies and animal models, and reinforce the clinical utility of noncontact specular microscopy in uveitis care and preoperative assessment.

Comparison with previous studies. Alfawaz et al. (Ophthalmology, 2016) reported significantly lower ECD and reduced HEX% in uveitic eyes compared to controls and found correlations between ECD and duration/flare measurements, consistent with our findings.[8] Pillai et al. (Br J Ophthalmol, 2000) used specular microscopy to show localized endothelial disruption in proximity to KPs with partial recovery after inflammation resolution — echoing our association between KPs and lower ECD.[7] Oliviera et al. (2009) and Guclu et al. (2019) also reported decreased ECD and altered morphometrics in infectious and noninfectious uveitis cohorts, indicating that endothelial involvement is broadly seen across etiologies.[9–12] Trinh and colleagues demonstrated in an endotoxin-induced uveitis model that immune activation and endothelial antigen expression accompany endothelial morphological change — providing mechanistic plausibility for the clinical observations.[10]

Our observation that active inflammation causes greater endothelial compromise than quiescent disease supports longitudinal data and meta-analytic syntheses (e.g., Mejía-Salgado et al., 2024), which report consistent ACI-associated reductions in ECD and HEX% and increases in CV/CCT.[11] Clinically, this suggests that inflammation control is likely to reduce ongoing endothelial injury and should inform timing of intraocular procedures. Case series in Behçet's disease and Fuchs' uveitis have also documented persistent endothelial alterations even during inactivity, suggesting that repeated or severe attacks may yield semi-permanent endothelial loss.[6 13]

Mechanisms and clinical implications.
Inflammatory cytokines (IL-1, TNF-α), leukocyte adhesion molecules, and direct cytotoxic mechanisms can lead to endothelial cell apoptosis or functional disturbance.[14] Animal EIU models confirm endothelial activation, leukocyte adhesion and antigen expression, consistent with human specular/confocal results.[10] Functionally, decreased ECD and increased polymegathism lower the cornea's reserve to tolerate additional surgical trauma. Therefore, in uveitic patients being considered for cataract or glaucoma surgery, pre-operative specular microscopy is prudent: low ECD, high CV, and low HEX% should prompt discussion of heightened risks of postoperative decompensation and consideration of modified surgical plans.[12 15]

Strengths and limitations. Strengths include strict inclusion/exclusion criteria, use of established SUN grading, and single-operator specular imaging to limit variability. Limitations include cross-sectional design (no longitudinal follow up to assess recovery or progression), moderate sample size, and use of a single central measurement rather than peripheral mapping. Different specular microscope models and software algorithms can yield interdevice variability — a methodological caveat when comparing absolute numbers across studies.[12 16]

Future directions. Prospective longitudinal studies tracking endothelial recovery after inflammation control, and studies evaluating the predictive value of preoperative endothelial metrics for post-operative corneal outcomes in uveitic eyes, are needed. Investigations using confocal microscopy or molecular markers may elucidate mechanisms of endothelial injury and repair.

CONCLUSION

In this comparative cross-sectional study, anterior uveitis was associated with reduced endothelial cell density, increased polymegathism, decreased hexagonality and mild increases in central corneal thickness, with active inflammation showing the worst metrics. Non-contact specular microscopy is a practical, noninvasive tool for quantifying endothelial health in uveitis and should be integrated into routine assessment and pre-surgical planning. Future longitudinal work should assess the reversibility of these changes with inflammation control and the predictive value of baseline endothelial metrics for surgical outcomes.

AUTHOR CONTRIBUTIONS

Dr Srilekha R M — conceptualization, data acquisition, manuscript drafting
Dr Chaitra MC — supervision, methodology, manuscript revision
Srishti Yadav — data collection and entry, literature review.
All authors approved the final manuscript.

FUNDING

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ETHICS

Approved by the Central Ethical Committee, Sri Devaraj Urs Medical College. Written informed consent was obtained from all participants.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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