Original Article

Corneal endothelium in unilateral Fuchs heterochromic iridocyclitis

N Geetha Sravani[#], Ashik Mohamed[#], Sunita Chaurasia[1], Shravya Sri Durgam, Somasheila I Murthy[1]

Purpose: To assess the corneal endothelium in patients with Fuchs heterochromic iridocyclitis (FHI) and compare it with the normal fellow eye. **Methods:** Retrospective, observational, cross-sectional study of 31 patients seen between Jan 2016 to Dec 2018, with clinical diagnosis of Fuchs heterochromic iridocyclitis, was performed. Specular microscopic examination was documented in both eyes. The affected eyes formed the study group and the fellow healthy eyes served as controls. **Results:** The mean age of the patients was 29.9 ± 8.2 years. The endothelial cell density (P = 0.0001) was significantly lower, whereas average cell size (P = 0.0001), coefficient of variation (P = 0.004), and maximum cell area (P = 0.01) were significantly higher in the affected eye compared to the control eye. In three patients, the affected eye showed guttae, while the healthy fellow eye revealed a normal specular mosaic. **Conclusion:** Specular microscopic analysis shows endothelial alterations in the affected eyes in FHI.

Key words: Corneal endothelium, fuchs heterochromic iridocyclitis, specular microscopy

Access this article online

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_869_19

Quick Response Code:

Fuchs heterochromic iridocyclitis (FHI) or the more recent designation Fuchs Uveitis Syndrome (FUS) is a disease characterized by low grade chronic anterior chamber inflammation with good visual prognosis.[1,2] Several viruses such as Herpes Simplex Virus, Cytomegalovirus, Chikungunya virus, and Rubella virus have been implicated as causative agents.[3-6] The condition is predominantly unilateral with no strong gender predilection and occurs over a wide age range with most patients presenting in the third and fourth decade of life.

The clinical findings described in FHI are heterochromia, iridocyclitis, cataract, glaucoma, and vitritis. Even though the nomenclature includes heterochromia, difference in the iris color compared to the fellow eye may or may not be observed. Similarly, vitreous opacities and chorioretinal scars can occur and hence the terminology iridocyclitis is not entirely accurate. The anterior uveitis in this condition is typically characterized by diffuse or stellate keratic precipitates or pigments on corneal endothelium and absence of synechiae.[7] At this point of time, the underlying cause is uncertain and the diagnosis is essentially made on clinical grounds.

Chronic anterior segment inflammation and uveitis are known to affect corneal endothelium variably. Alfawaz *et al*. reported changes in the corneal endothelium in eyes with anterior uveitis.[8] FHI is a good model to study the endothelial changes in anterior uveitis as the disease is predominantly unilateral; hence, the fellow eye can serve as a control for comparative analysis. The purpose of this study was to assess the corneal endothelium in patients with unilateral FHI by using specular microscopy and compare it with the normal fellow eye.

Methods

The Institutional Ethics Committee approved the conduct of the study and the study adhered to the tenets of the Declaration of Helsinki. An informed consent was taken from the study participants. The study was a retrospective, observational, cross-sectional study. During the time period Jan 2016 to Dec 2018, a total of 31 patients were included in the study. The inclusion criteria included patients with only uniocular FHI [Fig. 1], without any prior intraocular intervention and who had specular microscopic examination documented in both eyes. The fellow eye was evaluated to rule out the ocular pathologies that could affect the endothelial imaging. The unaffected fellow eye was considered as an age-matched control.

Specular microscopy was used to assess the corneal endothelium (Specular Microscope EM-3000, Tomey, Nagoya, Japan). A single image was captured from the central corneal endothelium of each eye and the same was used for analysis. The quantitative parameters studied were corneal endothelial cell density (ECD), number of cells, cell density, average cell area, coefficient of variation, maximum cell area, and minimum

Department of Ophthalmic Biophysics and [1]Cornea and Anterior Segment Services, L V Prasad Eye Institute, Hyderabad, Telangana, India

[#]The first two authors have contributed equally to this work

Correspondence to: Dr. Sunita Chaurasia, Cornea and Anterior Segment Services, L V Prasad Eye Institute, L V Prasad Marg, Banjara Hills, Hyderabad - 500 034, Telangana, India. E-mail: sunita@lvpei.org

Received: 03-May-2019 Revision: 19-Jun-2019
Accepted: 24-Sep-2019 Published: 14-Feb-2020

Cite this article as: Sravani NG, Mohamed A, Chaurasia S, Durgam SS, Murthy SI. Corneal endothelium in unilateral Fuchs heterochromic iridocyclitis. Indian J Ophthalmol 2020;68:447-9.

cell area. All the measurements were taken from the central clear area of the cornea.

Statistical analysis was performed using the software Origin v7.0 (OriginLab Corporation, Northampton, MA, USA). The data were checked for the normality of distribution using Shapiro-Wilk Normality Test. All continuous data were not normally distributed and were described in terms of median and inter-quartile range (IQR). Categorical data were described in proportions. Paired *t*-test or Wilcoxon signed-rank test was used to compare the continuous data between FHI and control eyes depending on the normality of distribution and homoscedasticity (assessed by Levene test). Mann-Whitney test was performed to assess the relationship between the presence of anterior chamber inflammation and ECD. Spearman correlation was performed to assess the relationship of duration of uveitis and intraocular pressure with ECD. A *P* value of less than 0.05 was considered statistically significant.

Results

The mean age was 29.9 years ± 8.2 years. Twenty-two were males (70.96%) and nine were females (29.04%). The right eye was involved in 13 patients (41.9%) and the left eye in 18 patients (58.1%). The median visual acuity in the affected eyes was 0.69 (IQR, 0.30 to 1.79) and 0.00 (IQR, 0.00 to 0.00) in the control eyes. The mean central corneal thickness was 511.5 µm ± 44.1 µm in the affected eyes and 522.3 µm ± 39.3 µm in control eyes and the difference was not significantly different (*P* = 0.11).

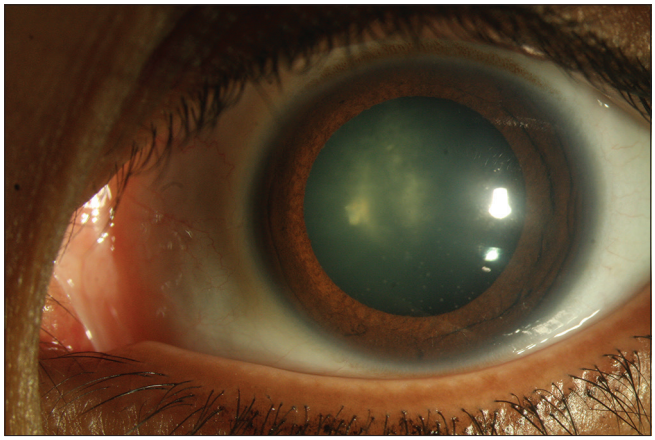

Figure 1: Cornea in Fuchs heterochromic iridocyclitis: This figure shows the slit lamp photograph of a patient with Fuchs heterochromic iridocyclitis having keratic precipitates

Majority (90%) of the patients presented to clinic with complaints of gradual decrease in vision over months to years. At the time when specular microscopy was performed, twenty (64.5%) eyes were documented to have trace to 1 + cells in the anterior chamber although none of the patients had complaints of pain or redness in the affected eye. Thirty eyes (96.8%) had characteristic stellate shaped keratic precipitates distributed in the inferior half of corneal surface and three (9.6%) eyes were noted to have heterochromia. Twenty-eight eyes (90.3%) had cataract and rest had clear crystalline lenses. The median intraocular pressure in the affected eye was 14 mm Hg (IQR, 12 to 16 mm Hg). None had any prior intraocular interventions at the time when specular imaging was done. None of the eyes had clinically apparent corneal edema.

Table 1 summarizes the specular microscopy data of the FHI eyes and their comparisons with the unaffected fellow eyes. The central corneal endothelial cell densities were significantly lower in the affected eye compared to the fellow eye. The estimated power for two-sample comparison of means in ECD in cells/mm^2 (n = 31; FHI eyes: 2209.9 ± 652.2; Control eyes: 2678.8 ± 310.8; two-sided α =0.05) was 95.1%. The average cell size, coefficient of variation, and maximum cell area were significantly higher in the affected eyes than the control eyes. Three patients, on clinical slit lamp examination, showed presence of guttae in the affected eye at all follow up visits while the fellow eye showed a completely normal endothelial morphology [Fig. 2]. Univariate analysis was performed to assess the effect of the presence of keratic precipitates and cells (P = 0.75), intraocular pressure (P = 0.97) and duration of history of complaints in affected eyes (P = 0.95) on endothelial cell density and none of them were found to be significantly affecting ECD.

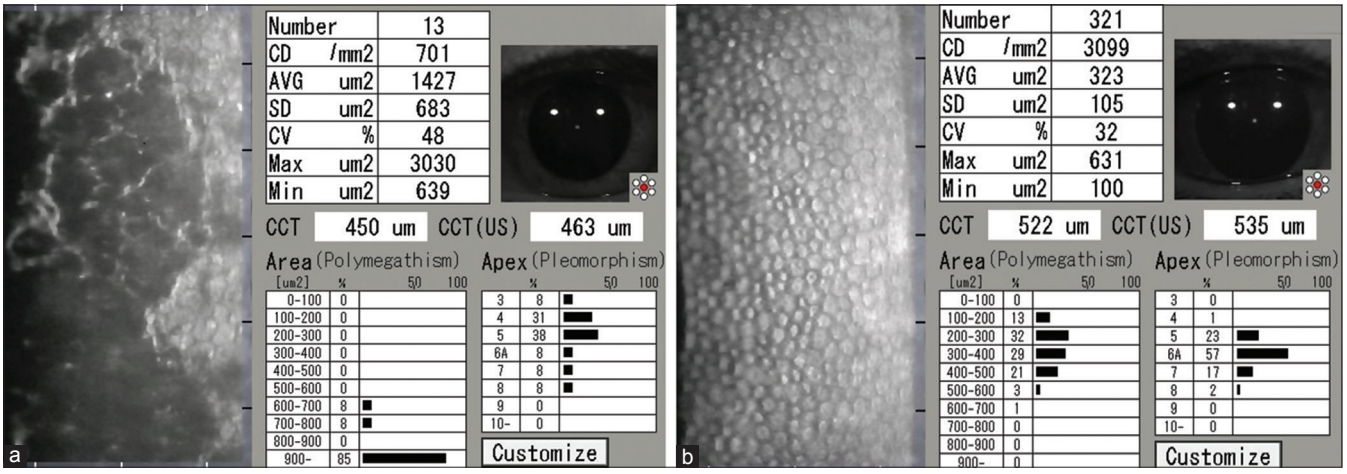

Figure 2: Specular microscopy in Fuchs heterochromic iridocyclitis: This figure shows the guttae noted on specular microscopy images of corneal endothelium from a patient with Fuchs heterochromic iridocyclitis (a) and a normal unaffected control eye (b)

Table 1: Analysis of quantitative parameters on specular microscopy imaging in patients with Fuchs heterochromic iridocyclitis (FHI). This table shows the comparison of specular microscopy results between FHI and controls (IQR: inter-quartile range)

Parameters	FHI (Affected eyes)	Control eyes	*P*
Number of cells, median (IQR)	212 (125-252)	269 (238-282)	0.0001
Endothelial cell density (mm^2), median (IQR)	2382 (2226-2619)	2707 (2551-2902)	0.0001
Average cell size (mm^2), median (IQR)	420 (382-449)	369 (345-392)	0.0001
Coefficient of variation %, median (IQR)	42 (39-47)	36 (33-40)	0.005
Maximum cell area (mm^2), median (IQR)	1283 (1042-2133)	783 (662-1139)	0.002
Minimum cell area (mm^2), median (IQR)	109 (92-128)	95 (81-103)	0.03

Discussion

The uveitis in FHI/FUS is typically low grade and can be chronic. The condition may be asymptomatic for long until the patient presents with decreased vision associated with cataract and characteristic distribution of keratic precipitates and other clinical signs supporting a diagnosis of FHI. There is a possibility of endothelial cell damage/loss in entities associated with chronic anterior segment inflammation.[9] Hence, we evaluated the corneal endothelium in FHI and compared this to healthy fellow eyes.

In a series of unilateral iridocylitis (n = 60) in European population, Setala reported reduced corneal endothelial cell densities in 8.3% of the eyes.[10] Alfawaz *et al*. reported central ECD to be lesser in unilateral uveitis eyes than the unaffected contralateral eyes.[8] In another study, endothelial cell density of eyes with FHI/FUS was significantly lower than control eyes.[11] Similar to previous studies, we found that the endothelial cell densities were reduced and mean cell area was increased significantly when compared to normal eye of the same patient. Our study had adequate power to differentiate the ECD between FHI eyes and control eyes.

In our study, we found three patients with guttae in corneal endothelium as evaluated on clinical slit lamp examination and "drop out areas" corresponding to guttae were captured on the specular imaging. The healthy fellow eyes of these patients were normal and revealed a normal endothelial specular mosaic ruling out the possibility of primary endothelial dystrophy. The formation of guttae is considered a stress response of the corneal endothelium. We feel that these changes are true guttae in Descemet membrane as these were noted at multiple follow up visits of the patient and did not resolve at any point of time. Even though this observation isn't surprising, it is noteworthy as previous studies have not reported this association.

Conclusion

Corneal endothelial changes are reported in patients with anterior uveitis. However, there are limited studies of endothelial affliction in relation to FHI/FUS. Our study supports the alterations in corneal endothelium in FHI/FUS.

Financial support and sponsorship

Hyderabad Eye Institute and Hyderabad Eye Research Foundation.

Conflicts of interest

There are no conflicts of interest.

References

1. Cunningham ET Jr, Baglivo E. Fuchs heterochromic iridocyclitis - Syndrome, disease, or both? Am J Ophthalmol 2009;148:479-81.
2. Rothova A. The riddle of Fuchs heterochromic uveitis. Am J Ophthalmol 2007;144:447-8.
3. Goldstein DA, Mis AA, Oh FS, Deschenes JG. Persistent pupillary dilation in herpes simplex uveitis. Can J Ophthalmol 2009;44:314-6.
4. Chee SP, Jap A. Presumed Fuchs heterochromic iridocyclitis and posner-schlossman syndrome: Comparison of cytomegalovirus-positive and negative eyes. Am J Ophthalmol 2008;146:883-9.
5. Babu K, Murthy GJ. Chikungunya virus iridocyclitis in Fuchs' heterochromic iridocyclitis. Indian J Ophthalmol 2012;60:73-4.
6. Quentin CD, Reiber H. Fuchs heterochromic cyclitis: Rubella virus antibodies and genome in aqueous humor. Am J Ophthalmol 2004;138:46-54.
7. Babu K, Adiga M, Govekar SR, Kumar BR, Murthy KR. Associations of Fuchs heterochromic iridocyclitis in a South Indian patient population. J Ophthalmic Inflamm Infect 2013;3:14.
8. Alfawaz AM, Holland GN, Yu F, Margolis MS, Giaconi JA, Aldave AJ. Corneal endothelium in patients with anterior uveitis. Ophthalmology 2016;123:1637-45.
9. Trinh L, Brignole-Baudouin F, Labbé A, Raphaël M, Bourges JL, Baudouin C. The corneal endothelium in an endotoxin-induced uveitis model: Correlation between *in vivo* confocal microscopy and immuno histochemistry. Mol Vis 2008;14:1149-56.
10. Setälä K. Corneal endothelial cell density in iridocyclitis. Acta Ophthalmol (Copenh) 1979;57:277-86.
11. Szepessy Z, Tóth G, Barsi Á, Kránitz K, Nagy ZZ. Anterior segment characteristics of fuchs uveitis syndrome. Ocul Immunol Inflamm 2016;24:594-8.