Comparative assessment of the corneal endothelium following phacoemulsification surgery in patients with type II diabetes and nondiabetes

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Abstract:

PURPOSE: The purpose is to assess the corneal endothelial changes after phacoemulsification surgery in diabetic patients and compare with those of nondiabetic subjects.

METHODS: The study compared the corneal endothelial changes in diabetics and nondiabetics after phacoemulsification surgery. The study population included 40 patients with diabetes mellitus with good glycemic control and 40 nondiabetic patients who underwent uneventful phacoemulsification surgery. Central corneal endothelial cell density (ECD), central corneal thickness (CCT), and percentage of hexagonality percentage coefficient of variation (%CV) were measured preoperatively and postoperatively (at 4 and 12 weeks) using a specular microscope.

RESULTS: Mean ECD loss (%) was measured as 9.85% and 8.41% at 4 weeks and 12 weeks postoperatively in the diabetic group while ECD loss percentage was 7.09% and 5.74% in the control group at the same time intervals, respectively. Furthermore, a significant difference was noted on comparing mean ECD measurements between the two groups at the postsurgical visits (4 weeks and 12 weeks). While the CCT was found to be similar in both diabetic and nondiabetic patients, increase was observed in the values of (%CV in both the groups at postoperative 4 weeks' and 12 weeks' follow-up. The values of both %CV and percentage hexagonality showed statistically significant differences between the diabetic and nondiabetic group before surgery and at 4 weeks' and 12 weeks' postoperative examinations.

CONCLUSION: The patients with diabetes suffered greater endothelial damage despite good glycemic control as compared to nondiabetic patients which indicates the necessity of far more care to protect cornea endothelium in patients with diabetes.

Keywords:

Corneal endothelium, diabetes mellitus, endothelial cell density, phacoemulsification

Introduction

Cataract is one of the major avoidable causes of blindness worldwide.[1] Phacoemulsification, a surgery performed to treat cataract provides better vision to patients although, it may also lead to corneal endothelial cell loss as a result of ultrasound energy employed.[2] A healthy corneal endothelium is critical in maintaining corneal hydration and transparency.

The corneal endothelial cell count keeps on decreasing with age and this decline is accelerated in systemic diseases such as diabetes and following surgical procedures.[3] Loss of endothelial cells may lead to corneal edema which in turn may progress to corneal decompensation and vision loss.[4] A minimal endothelial cell density (ECD) of 400–500 cells/mm^2 is essential for maintaining the pumping activity of the corneal endothelium.[5] Safeguarding the endothelium is therefore crucial during phacoemulsification, especially in old-age patients with diabetes.

Diabetes mellitus (DM) damages the corneal endothelial cells which undergo morphological alterations such as polymegathism and pleomorphism owing to the minimal

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regenerative capacity of these cells.[6] Although the exact mode through which diabetes induces endothelial damage is not known, few studies suggest that aggregation of advanced glycation end products within endothelial cells is responsible for oxidative stress and damage to these cells.[12] Furthermore, chronic hyperglycemia inhibits the Na-K ATPase pump which in turn disrupts endothelial pump function in diabetes.[7,13] Furthermore, diabetic cataract formation also occurs as a result of the accumulation of reactive oxygen intermediates.[8]

The corneal endothelium can be assessed using specular microscopy through four parameters: central corneal thickness (CCT), ECD, coefficients of variance (CV), and percentage hexagonality.[9,14] The CCT is indicative of the endothelial cell function.[15] The CV indicates variability in the cell size whereas percentage hexagonality refers to variation in the hexagonal cells shape.[16] Both CV and hexagonality denote the recovery process of the corneal endothelium.[10]

Past studies have reported differing values of endothelial loss after phacoemulsification surgery. The mean endothelial loss in different studies has been found to range between 6% and 22% in patients with diabetes and 1%–11% in nondiabetic patients.[19,21-25] The main culprits behind endothelial damage are advancing age, greater use of ultrasound energy, and increased phaco time.[24] The cornea in diabetic patients tends to suffer even greater damage owing to complications arising as a result of a greater degree of inflammation, defective recovery, and poor endothelial functional reserve.[14]

The postoperative visual recovery following cataract surgery is dependent on the condition of cornea. It is proposed that phacoemulsification may cause greater damage to the cornea in patients with diabetes, although the exact degree and perpetual changes that may transpire following phacoemulsification in diabetic cornea remains doubtful.[11] Hence, this study aimed to assess the corneal endothelium in diabetic patients following phacoemulsification surgery.

Methods

This was a prospective case–control study conducted in the department of ophthalmology from March 2018 to January 2019. The study was approved by ethical committee of BRD Medical College and informed consent was obtained from all participants of the study.

Inclusion criteria

The study subjects were divided into two groups: the diabetic group included patients with type 2 diabetes, aged between 50 and 70 years with good glycemic control (HbA1c <7) and grade I, II, or III nuclear sclerosis who underwent phacoemulsification surgery. Nondiabetic control group included patients of the same age group who underwent phacoemulsification surgery during the same time. All diabetic patients were evaluated for serum glycosylated hemoglobin (HbA1c) levels to assess their glycemic control.

Exclusion criteria

Patients with a history of previous ocular surgery, uveitis or ocular inflammation, corneal opacities, glaucoma, ocular trauma, pseudoexfoliation, nuclear sclerosis grade IV, or any history of treatment with glucocorticoids, were excluded from the study.

Study population

The study population included 40 eyes of 40 diabetic patients with good glycemic control and 40 eyes of 40 nondiabetic patients as controls.

Patient examination

All patients included in this study underwent complete ophthalmic evaluation preoperatively including visual acuity, slit-lamp examination, tonometry, and posterior segment examination under full pupillary dilation. Cataract grading was done using Lens Opacities Classification System III (LOCS III).[27] ECD, CCT, percentage hexagonality, and %CV were noted preoperatively and 4 weeks and 12 weeks postoperatively with the help of Topcon SP-1P Specular Microscope (Topcon Corporation, Tokyo, Japan).

Surgical technique

All the patients were administered eye drop moxifloxacin 0.5% preoperatively 1 day before surgery and pupillary dilatation was done using tropicamide 0.8% and phenylephrine 5% eye drop. All surgeries were performed under local anesthesia. Phacoemulsification and implantation of an intraocular lens were performed by a single-experienced surgeon using Oertli CataRhex (Oertli Switzerland) phaco machine.

The intraoperative procedure included creating a 2.80 mm clear corneal incision using 2.80 mm keratome and a paracentesis incision with the help of microvitreoretinal blade, followed by injection of a viscoelastic substance (hydroxypropyl methylcellulose 2%) in the anterior chamber. Continuous curvilinear capsulorhexis was made and hydrodissection and nuclear rotation were done. Nucleotomy and phacoemulsification of nuclear fragments was performed followed by bimanual aspiration of residual cortical matter from the capsular bag. Intraocular lens was implanted within the capsular bag in all the patients. All patients received a combination of an antibiotic and a steroid postoperatively for 4 weeks.

Statistical analysis

Data collected from the participants were compiled into MS Excel and further analyzed statistically using R STUDIO Version 4.2.2 (R Studio, Boston, MA, USA). The study results were statistically analyzed using independent sample *t*-test. The pre- and postsurgical ECD, CV, hexagonality, and CCT values between the two groups were compared using unpaired *t*-test. Comparison within the groups was done using paired sample *t*-test. The result was considered statistically significant if $P < 0.05$.

Results

A total of 80 eyes from 80 patients were included in this study.

Forty patients in a diabetes study group and 40 patients in nondiabetic control group, both groups had grade I-III cataracts according to LOCS III.

The overall mean age of the study population was 59.00 ± 5.23 years in the range of 51–69 years. The mean age of diabetes patients was 58.92 ± 4.87 years and that of nondiabetic patients was 59.08 ± 5.63 years. The two groups were alike as regards age and sex distribution and no statistically significant difference was noted (*P* = 0.160 and *P* = 0.361, respectively). The difference between mean preoperative axial length, anterior chamber depth, and cataract grade was also not significant between the two groups. The mean duration of diabetes was 7.35 ± 3.29 years in the study group. Table 1 summarizes the baseline characteristics of the two groups.

Presurgical and postsurgical measurements at (4 weeks and 12 weeks) for the ECD, CCT, coefficient of variation, and hexagonal cell percentage between groups are enumerated in Table 2. The pre- versus postoperative cell measurements within the groups are illustrated in Table 3.

Table 1: Baseline characteristics of diabetic and control groups

Characteristics	Diabetic (*n*=40)	Nondiabetic (*n*=40)	*P*
Age (years), mean±SD	58.92±4.87	59.08±5.63	0.160
Gender			
Male	26	22	0.361
Female	14	18	
Eye			
Right	17	21	0.370
Left	23	19	
ACD (mm) (preoperatively)	3.46±0.38	3.55±0.32	0.265
Axial length (mm) (preoperatively)	23.10±0.54	23.16±0.53	0.372
Cataract grade			
I	8	7	0.661
II	17	14	
III	15	19	

SD: Standard deviation, ACD: Anterior chamber depth

The values of mean preoperative ECD were not statistically different between the diabetic and control groups (2381.45 ± 143.35 and 2406.13 ± 166.12, respectively; *P* = 0.479). The ECD values showed a decline of 232.68 (standard deviation [SD] 33.69) in the diabetes group and 169.90 (SD 21.40) in the control group by the end of 12 weeks. This decline was found to be statistically significant (*P* < 0.001) on intragroup comparison. Furthermore, a significant difference was noted on comparing mean ECD measurements between the two groups at the postoperative (4 and 12 weeks) evaluations (*P* = 0.027 and *P* = 0.022, respectively). Further, it was observed that the mean ECD values kept on decreasing at each follow-up examination postoperatively. The mean ECD loss percentage (%) was estimated as 8.41% and 9.85% at 4 weeks and 12 weeks postoperatively, respectively, in the diabetic group, while it was 5.74% and 7.09% in the control group at the same time points, respectively. Figure 1 indicates ECD changes following phacoemulsification.

The CCT was found to be similar in both diabetic and nondiabetic subjects. There was no statistically significant difference between the two groups before the surgery and also after the surgery at 4 weeks and 12 weeks (*P* = 0.817, *P* = 0.059, and *P* = 0.160, respectively).

The %CV increased in both the groups at postoperative 4 weeks and 12 weeks' follow-up visits. The values of %CV showed statistically significant differences between the diabetic and nondiabetic group, both before surgery and at 4 weeks and 12 weeks' postoperative evaluation (*P* = 0.044, *P* = 0.007, and *P* = 0.008, respectively). The mean CV values were lower in the nondiabetic subjects as compared to patients with diabetes. The variation from baseline was found to be statistically significant

Table 2: Pre- and postoperative measurements in diabetic and nondiabetic control groups

	Mean±SD		*P**
	Diabetic group (*n*=40)	Nondiabetic control group (*n*=40)	
Endothelial cell density (cells/mm²)			
Preoperative	2381.45±143.35	2406.13±166.12	0.479
Postoperative at 4 weeks	2183.15±163.79	2269.18±176.40	0.027
Postoperative at 12 weeks	2148.78±165.09	2236.22±168.89	0.022
CCT (μ)			
Preoperative	520.43±13.03	521.13±13.97	0.817
Postoperative at 4 weeks	535.03±10.93	529.88±13.0	0.059
Postoperative at 12 weeks	529.00±11.36	525.10±13.15	0.160
CV			
Preoperative	36.23±3.18	34.98±2.18	0.044
Postoperative at 4 weeks	42.38±3.39	40.52±2.57	0.007
Postoperative at 12 weeks	39.73±3.27	38.02±2.27	0.008
Hexagonality			
Preoperatively, % cells (SD)	48.35±2.21	49.63±3.01	0.034
Postoperatively, % cells (SD) at 4 weeks	43.98±2.45	44.85±2.78	0.140
Postoperatively, % cells (SD) at 12 weeks	45.50±2.35	47.23±2.72	0.003

*Independent *t*-test. SD: Standard deviation, CCT: central corneal thickness, CV: Coefficient of variance

Table 3: Mean changes within the groups in cell measurements 4 weeks and 12 weeks postoperatively

Cell parameters	Diabetic group (*n*=40)		Nondiabetics group (*n*=40)	
	Mean change±SD (%)	*P*	Mean change±SD (%)	*P**
Endothelial cell loss (cells/mm²)				
Preoperative/4 weeks	198.30±32.72	0.000	136.95±22.21	0.000
Preoperative/12 weeks	232.68±33.69	0.000	169.90±21.40	0.000
CV (%)				
Preoperative/4 weeks	−6.15±1.39	0.000	−5.55±0.71	0.000
Preoperative/12 weeks	−3.50±1.09	0.000	−3.05±0.64	0.000
Hexagonality (%)				
Preoperative/4 weeks	4.38±1.00	0.000	4.78±1.87	0.000
Preoperative/12 weeks	2.85±0.95	0.000	2.40±1.24	0.000
CCT (μ)				
Preoperative/4 weeks	−14.6±1.00	0.000	−8.75±2.62	0.000
Preoperative/12 weeks	−7.35±9.82	0.000	−3.95±1.80	0.000

*Paired sample *t*-test. CV: Coefficient of variation, CCT: central corneal thickness, SD: Standard deviation

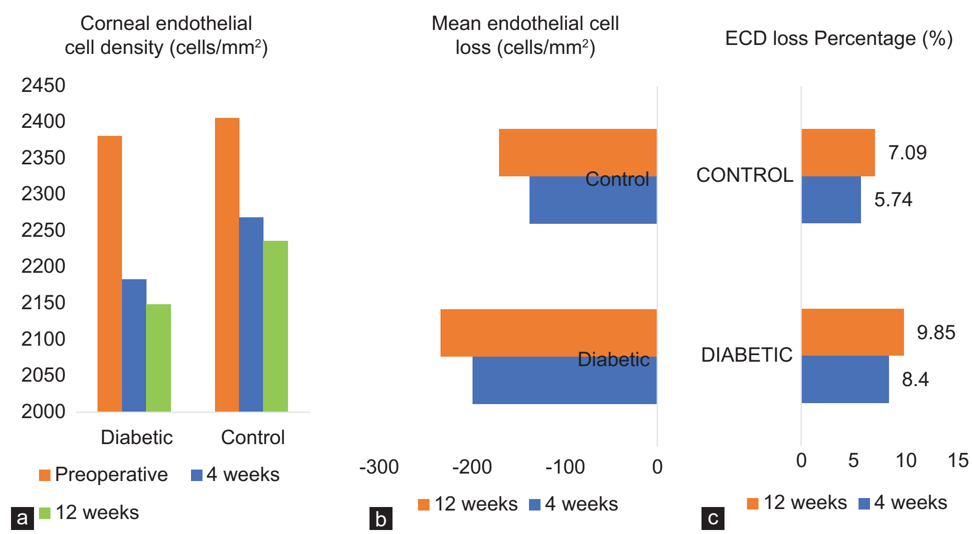

Figure 1: Endothelial cell density (ECD) changes after phacoemulsification (a) Mean ECD preoperative, at 4 weeks and 12 weeks postoperatively, (b) Mean endothelial cell loss at 4 weeks and 12 weeks postoperatively, (c) ECD loss percentage at 4 weeks and 12 weeks postoperatively

within the groups on intragroup comparison, at all times of examination ($P < 0.001$). The peak change in % CV was noted at 4 weeks postoperatively in both the groups.

We further observed significant differences in the mean percentage hexagonality values between the two groups, both preoperatively and at 12 weeks postoperatively ($P = 0.034$ and $P = 0.003$, respectively). The values of percentage hexagonality were lower in the diabetic group. The changes from baseline were found to be statistically significant within the groups on intragroup comparison, at 4 weeks and 12 weeks' postoperative visit ($P < 0.001$). In patients with diabetes, the mean change from baseline was −4.38% and −2.85% at 4 weeks and 12 weeks' intervals, respectively ($P < 0.001$). Figure 2 illustrates measurements of CCT, CV, hexagonality preoperatively and at 4 weeks and 12 weeks postoperatively.

Subgroup analysis of endothelial cell parameters in relation to the duration of DM revealed that ECD, CV, and CCT values in diabetic patients having DM for 10 years or more were significantly different from the group of patients having diabetes for 10 years or less. Figure 3 indicates endothelial cell parameters of diabetic patients and controls in relation to the duration of DM.

Discussion

The study aimed to evaluate the effects of phacoemulsification cataract surgery on corneal endothelium in patients with type 2 DM and compare it with those of nondiabetic subjects.

Corneal endothelial cells are important for maintaining corneal hydration and transparency by means of Na-K ATPase pump. When ECD decreases, the adjacent cells expand and become enlarged (polymorphism) and nonhexagonal (pleomorphism).[12] Various studies suggest diabetes causes decreased hexagonality and increased CV of corneal endothelium cells while some studies suggest no such effect on the endothelium.[20-22] Taşlı *et al*. in their study found that ECD and hexagonal cell ratio were lower while average cell size, %CV, and CCT were higher in diabetic patients.[17]

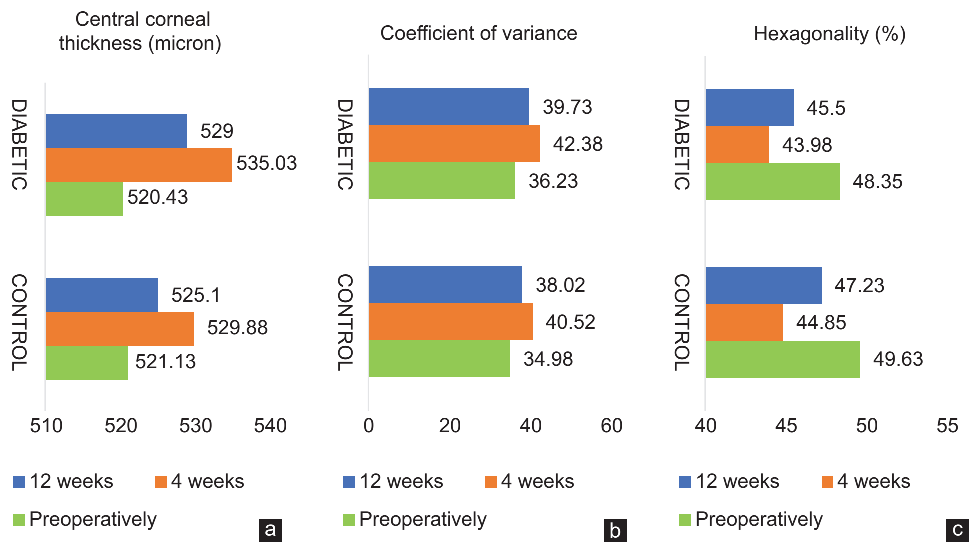

Figure 2: Measurements of (a) central corneal thickness, (b) coefficient of variance, (c) Hexagonality preoperatively and at 4 weeks and 12 weeks postoperatively

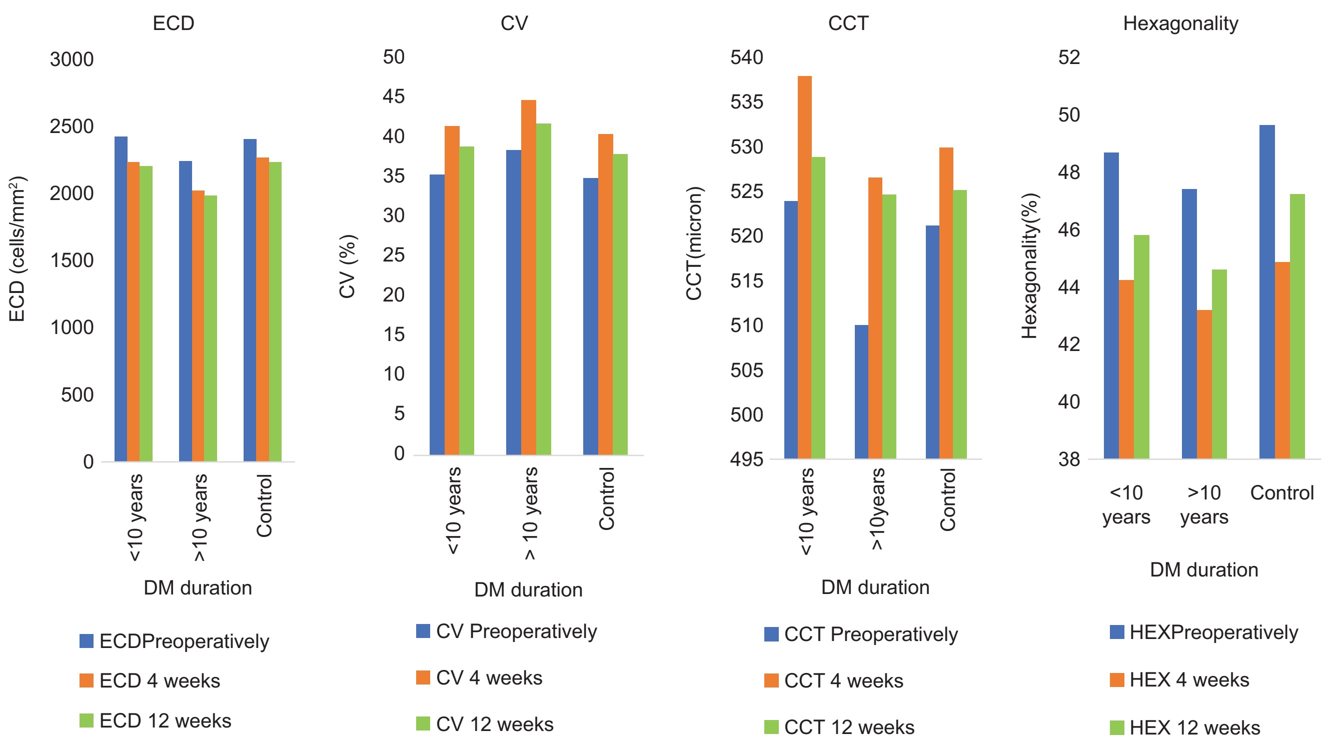

Figure 3: Endothelial cell parameters of diabetic patients and controls in relation to duration of diabetes mellitus (DM) (P = independent sample t-test) endothelial cell density, coefficient of variation, and central corneal thickness values in diabetic patients having DM for 10 years or more were significantly different from group of patients having diabetes from 10 years or less. ECD: Endothelial cell density, CV: Coefficient of variation, CCT: central corneal thickness

The corneal endothelial cell changes in diabetes may occur as a result of dysfunctional apical junctions in endothelial cells, defective permeability due to decreased Na-K ATPase pump function, and altered tight junctions and desmosomes in corneal endothelial cells.[13,14,29] Further, hyperglycemia leads to a surge in the aldose reductase pathway which causes sorbitol aggregation within the endothelial cells, as a result of which corneal edema may ensue.[28] Studies have suggested that cataract surgery compromises diabetic corneas as a result of the altered response to surgical stress and diminishing functional reserve and poor healing.[15,16,18]

In this study, the preoperative ECD in the diabetic and control groups was similar. This is in agreement with studies such as Kudva *et al*. and Hugod *et al*.[20,21] Although postoperative endothelial cell loss after 12 weeks following phacoemulsification was significantly greater in diabetic patients as compared to nondiabetic patients. This finding is similar to the observations of Hugod *et al*. and contrary to the findings of Beato *et al*.[22] This difference in observations could be due to variations in sample sizes, duration, and control of diabetes in study subjects. The mean ECD loss (%) in our study was reported to be 9.85% at 12 weeks postoperatively in the diabetic patients while it was 7.09% in normal patients. A study by He *et al*. observed endothelial cell loss of 15% postcataract surgery as compared to 11% in normal patients.[19]

In our study, a significant difference was observed in mean ECD values between preoperative and postoperative (4 and 12 weeks) follow-up evaluation within each group, and a significant difference was also evidenced on comparing mean ECD values between the two groups both at pre- and postsurgical examinations. ECD loss in normal patients may be attributed to cell injury owing to surgical procedure although greater endothelial cell loss was observed in diabetic patients as compared to nondiabetic patients. Hugod *et al*. in their study reported endothelial cell loss of 6.2% in the diabetic group and 1.4% in the nondiabetic patients whereas mean ECD showed no significant difference between the diabetic and control group in the study by Fernández-Muñoz *et al*.[21,26]

The values of the coefficient of variance measured both presurgically and postsurgically showed significant differences between both the groups. Furthermore, the percentage of hexagonal cells was significantly lower in diabetic patients as compared to controls, at both presurgical and 12 weeks' postoperative evaluation. This observation takes precedence as diabetic corneas have coexisting structural and functional abnormalities. Polymegathism (%CV) and pleomorphism (percentage hexagonality) are indicative of these abnormalities. Furthermore, corneal pachymetry measurements (CCT) showed no statistically significant difference between the two groups, both pre- and postoperatively. However, a significant difference was observed for the increase in CCT in both diabetics and normal patients.

A meta-analysis by Yang *et al*.[10] evaluated 13 studies and they observed that CCT and CV were significantly higher and hexagonality was significantly lower in the diabetic group at 1 month though no significant difference in CV and hexagonality was noted at 3 months and 6 months between both the groups. They also noticed that ECD values were lower in diabetic patients as compared to nondiabetic patients at all postoperative times.[10] Another study by Chaurasia *et al*. detected a higher %CV and lower percentage hexagonality in patients with diabetes at all follow-up examinations.[25]

It is important to emphasize that, in this study, progressive endothelial cell loss was noted in both the groups from 4 weeks to 12 weeks' postoperative examinations, however, the diabetic patients experienced a greater degree of endothelial loss as compared to normal controls. We also observed that the postoperative CCT values were not significantly different between the groups. Thus, diabetic corneas may be able to function normally despite experiencing greater degree of endothelial cell loss and having higher coefficient of variance.

We noted few limitations in our study such as low sample size, and shorter duration of postoperative follow-up of the patients in both the groups. We also did not consider the effect of effective phaco time on corneal endothelium in our study.

Conclusion

The study concludes that the corneal endothelium undergoes deleterious modifications in diabetes. Corneal endothelium loss greatly increases following cataract surgery. These damaging effects are more in diabetic patients than healthy individuals. Diabetes may decrease corneal ECD and the percentage of hexagonal cells, but increases coefficient of variance, indicating that the corneal endothelial cells in these patients become more unstable. Surgeons, therefore, should try to preserve corneal endothelium during cataract surgery, more so in case of diabetic patients.

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Conflicts of interest

There are no conflicts of interest.

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