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Endothelial Cell Loss and Central Corneal Thickness in Patients With and Without Diabetes After Manual Small Incision Cataract Surgery

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Purpose: Cataract surgery is known to change the corneal endothelial cell density and morphology. In patients with diabetes, this change is more pronounced. This prospective cohort study was conducted to assess and compare the endothelial cell loss and change in central corneal thickness (CCT) after manual small incision cataract surgery (SICS) in patients with diabetes versus age-matched patients without diabetes.

Methods: Consecutive patients with diabetes (153) in the age group 40–70 years and age-matched patients without diabetes (163) undergoing manual SICS were enrolled. Preoperative and 1 week, 6 weeks, and 3 months postsurgery assessments of corneal endothelial loss and change in CCT were done using specular microscopy and ultrasound pachymetry.

Results: There was a steady drop in the endothelial density in both the groups postoperatively, with the percentage of endothelial loss at 6 weeks and 3 months being 9.26 ± 9.55 and 19.24 ± 11.57, respectively, in patients with diabetes and 7.67 ± 9.2 and 16.58 ± 12.9, respectively, in controls. The percentage of loss between 6 weeks and 3 months was found to be of significant difference ($P < 0.023$). In both the groups, an initial increase in CCT till the second postoperative week was followed by a reduction of CCT in the subsequent follow-up (sixth week) and a further reduction in the last follow-up (3 months). The change in CCT between the second and sixth weeks was significantly higher in the diabetic group ($P = 0.045$).

Conclusions: The diabetic endothelium was found to be under greater metabolic stress and had less functional reserve after manual SICS than the normal corneal endothelium.

Key Words: diabetes, manual small incision cataract surgery, specular microscopy, ultrasound pachymeter, pachymetry

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Changes in corneal epithelial and endothelial structure and function are commonly seen in diabetes mellitus (DM). DM can cause, inter alia, morphological changes in the epithelial cells, epithelial polymorphism, endothelial polymegathism, and stunting of surface microvilli. Increased endothelial polymegathism and pleomorphism and differences in the mean cell area and perimeter have been described in patients with diabetes. Patients with diabetes have been documented to have thicker corneas. They may also have a low endothelial reserve, making the endothelium more prone to stress-related injuries like ocular surgeries, despite a normal endothelial count.[1]

Schultz et al[2] had studied diabetic endothelium and found definite morphological changes in the endothelium like pleomorphism and polymegathism. But when compared with age-matched controls, they were not statistically significant. A study done by Shetlar et al[3] on endothelium of diabetic and nondiabetic corneal buttons used for keratoplasty showed no significant difference in endothelial morphology. However, an Indian study done by Saini and Mittal[4] showed a significantly lower corneal endothelial function in patients with type 2 diabetes with decompensation after deleterious stress.

Cataract surgery is one of the well-known factors that cause endothelial cell loss and corneal decompensation. All surgical procedures that involve entry into the anterior chamber damage a proportion of the endothelial cells as a result of intraoperative corneal manipulations. After endothelial cell loss, the adjacent cells enlarge and slide over to maintain endothelial cell continuity, which is observed as a change in the endothelial cell density and morphology. Moderate damage to the endothelium during surgery can also lead to a transient increase in the corneal thickness. Endothelial cell density and function can be assessed clinically using specular microscopy and pachymetry.

Studies done in the normal population to assess the response of the endothelium to cataract surgery have shown a decrease in the endothelial density (ED) over a 3-month period postoperatively, with an increase in the coefficient of variation and decrease in the percentage of hexagonal cells.[5,6] Morphological stability and functional integrity are necessary to maintain long-term corneal transparency after cataract surgery. Patients with diabetes have always been exempted from clinical trials assessing the effects of cataract surgery on the endothelium based on the assumption that they are more susceptible to damage during surgery. Only a few studies with controversial observations have been done, comparing the effect of cataract surgery on the corneal endothelium of patients with and without diabetes. Morikubo et al[7] did a similar study in patients undergoing small incision cataract surgery (SICS) by phacoemulsification and found that patients with diabetes suffered a statistically significant damage to endothelial cells and delayed recovery of postoperative corneal edema, although the coefficient of variation and the percentage of hexagonal cells did not vary much. While a study done by Furuse et al[8] showed no statistically significant difference in the endothelial cell loss and the coefficient of variation in both the groups after extracapsular cataract extraction. The increase in corneal thickness was significantly higher in patients with diabetes 1-month postoperatively when compared with patients without diabetes, showing a delayed recovery of corneal edema in the former.

Lee et al[9] studied the effect of the severity of retinopathy on endothelial loss postphacoemulsification and found an increased loss of endothelial cells and increased coefficient of variation in patients with high-risk proliferative diabetic retinopathy when compared with patients with nonproliferative diabetic retinopathy or patients without diabetes. In India, where the prevalence of cataract among the rural population is high, the socioeconomic issues favor manual SICS, which is more economical than the phacoemulsification technique. There is a paucity of data from India on the effect of SICS on the corneal endothelium. This study was undertaken to assess the postoperative endothelial cell loss and change in endothelial morphology and central corneal thickness (CCT) in patients with diabetes undergoing manual SICS and to compare them with age-matched nondiabetic individuals.

MATERIALS AND METHODS

Consecutive patients with type 2 DM (T2DM) in the age group 40–70 years and age-matched patients without diabetes undergoing manual SICS by experienced surgeons (more than 250 manual SICS) using the Blumenthal technique[10] between September 2006 and December 2007 were included in this prospective cohort study conducted in a tertiary teaching eye care center. Patients with preexisting corneal diseases, glaucoma, and uveitis and prior laser treatment were excluded from the study.

Sample Size

Endothelial cell loss was taken as the primary variable of this study, and a study done by Morikubo et al[7] as the baseline. The required sample for showing a significant difference, when the endothelial cell loss in patients with diabetes after SICS was 7.2% at the end of 1 month and in the patients without diabetes 3.25%, would be 188 in each arm with a power of 80% and a level of significance of 5%.

Methodology

Consenting patients underwent a complete preoperative ophthalmological examination, including best-corrected visual acuity using Snellen chart, refraction, slit-lamp biomicroscopy, applanation tonometry, gonioscopy, and dilated indirect fundus examination. Glycosylated hemoglobin (HbA_1C) level of patients with diabetes was checked for glycemic control. A clinical semiautomated noncontact specular microscope (Topcon SP 2000P) was used by the principal investigator alone to study endothelial cell details. Images were taken with low flash intensity in automatic mode using the variable frame analysis method to analyze central endothelial cell density. Two separate readings were taken, with the patient taking the chin off the chinrest and blinking once and returning to the examining position, and the average value was recorded as the measurement. The number of cells counted ranged from 70 to 100. Preoperative CCT was assessed using an ultrasound pachymeter (Tomey AL-1000) placed over the anesthetized cornea, with the patient looking straight ahead. An average of 3 readings to the nearest of 10 μm was taken.

Intraoperative details regarding pupillary dilation, use of dyes, type of capsulotomy, iris manipulation, type of intraocular lens (IOL) used, time taken for the surgery, and other complications were recorded. The patients were reviewed three times: between 2 and 3 weeks, 6–7 weeks, and 3 months postoperatively. At each visit, they had a complete ophthalmic examination, which included the best-corrected visual acuity, slit-lamp examination, and pachymetry. Specular microscopy was done only on the second and third visits. The grade of retinopathy was assessed on the second visit based on the Early Treatment Diabetic Retinopathy Study classification.[11] At the final visit, a repeat HbA1C was done along with a urine albumin test.

Statistical Analyses

SPSS 11.0 for Windows was used for analysis. Descriptive statistics such as mean ± SD, median (range), and frequency (percentage) were used to present continuous, continuous (skewed), and categorical variables, respectively. Comparisons of continuous variables between the groups were performed using independent sample '*t*' tests and Mann–Whitney tests. Association between categorical variables was assessed using χ^2 tests with Yates continuity correction. Relationships between variables were assessed using Pearson product moment correlation coefficient and were presented graphically using scatter plot. Appropriate graphs were used to present the data. A P value <0.05 was considered statistically significant.

RESULTS

A total of 158 eyes of 158 individuals with T2DM and 165 eyes of 165 normal individuals were studied. Five eyes of patients with T2DM and 3 eyes of normal individuals were excluded from the collected sample because of intraoperative changes made in the proposed surgical technique. All the patients were age matched in view of an association of the corneal ED with age. The average age of the normal

TABLE 1. Comparison of Corneal Parameters in Normal Individuals and Patients With T2DM Preoperatively

Parameters (Preoperatively)	Normal Individuals (n = 165)	Patients With T2DM (n = 158)
ED, cells/mm^2	1921 ± 322	2018 ± 349
Coefficient of variation	0.32 ± 0.58	0.34 ± 0.57
CCT, μm	503 ± 27	510 ± 31.3
No. eyes	163	153

TABLE 2. Comparison of Percentage of Endothelial Cell Loss in Normal Individuals and Patients With T2DM Postoperatively

Status	% EC Loss at 6 Weeks	% EC Loss Between 6 Weeks and 3 Months	% EC Loss at 3 Months
Normal individuals (n = 165)	7.67 ± 9.2	7.06 ± 9.33	16.58 ± 12.9
Patients with T2DM (n = 158)	9.26 ± 9.55	13.58 ± 11.27	19.24 ± 11.57

% EC loss = percentage of endothelial cell loss.

individuals was 60 ± 8.9 years (40–85 years) and that of patients with T2DM was 61 ± 9.18 years (42–85 years).

ED compared in the 2 groups did not show any statistical difference in different age groups. Because the groups were well age matched, the rest of the results were analyzed taking the cases and controls in all age ranges together. The preoperative corneal parameters were compared between the age-matched normal individuals and the patients with T2DM (Table 1). Patients with T2DM were found to have a significantly better ED than those with normal endothelium. The CCT was found to be higher in the diabetic population, which was statistically significant ($P < 0.02$). Table 2 shows the comparison of percentage of endothelial cell loss in normal individuals and patients with T2DM postoperatively. There was a steady drop in the ED seen in both the groups, postoperatively (Fig. 1). There was a statistically significant percentage loss in ED between 6 weeks and 3 months between the 2 groups. The coefficient of variation (CV) was found to gradually increase until the sixth postoperative week and then remain almost steady in both groups. There was no significant difference between the groups (Fig. 2). The change in CCT in the 2 groups postoperatively is given in Table 3. The CCT was found to be more in the diabetic population compared with the nondiabetic population throughout the postoperative period. The 6-week postoperative CCT was significantly higher in the patients with diabetes ($P < 0.25$) (Fig. 3).

The correlation of the grade of retinopathy with the percentage of endothelial cell loss at 3 months postoperatively showed a very minimal increase, which was not statistically significant (Fig. 4). Correlation of the grade of cataract with the percentage of endothelial cell loss at 3 months postoperatively revealed a small increase in the percentage of endothelial cell loss with an increasing grade of cataract, which was not statistically significant (Fig. 5). Table 4 shows the correlation of percentage of endothelial cell loss with duration of the surgery. There was an increase in the percentage of endothelial cell loss noted at the end of 3 months in patients who had a longer duration of surgery. But the difference was not statistically significant.

DISCUSSION

In developing countries like India, where there is a cataract backlog, manual SICS with IOL implantation promises to be a viable cost-effective alternative to phacoemulsification.[12] After every type of cataract surgery, with or without IOL implantation, the corneal endothelial cell count is diminished. Studies have found no significant difference in endothelial cell loss among the conventional extracapsular cataract extraction (ECCE), manual SICS, and phacoemulsification groups.[13] The endothelial response to cataract surgery is more evident in diabetic corneas because their endothelia have typical morphological characteristics.

A short-term (3-month postoperative) follow-up only was done because several studies have shown no change in the ED beyond 3 months. A study done by Schultz et al[5] to assess the response of endothelium to cataract surgery showed a decrease in the ED over 3 months postoperatively, with an increase in the coefficient of variation and decrease in the percentage of hexagonal cells. This was stabilized by 3 months. Another study

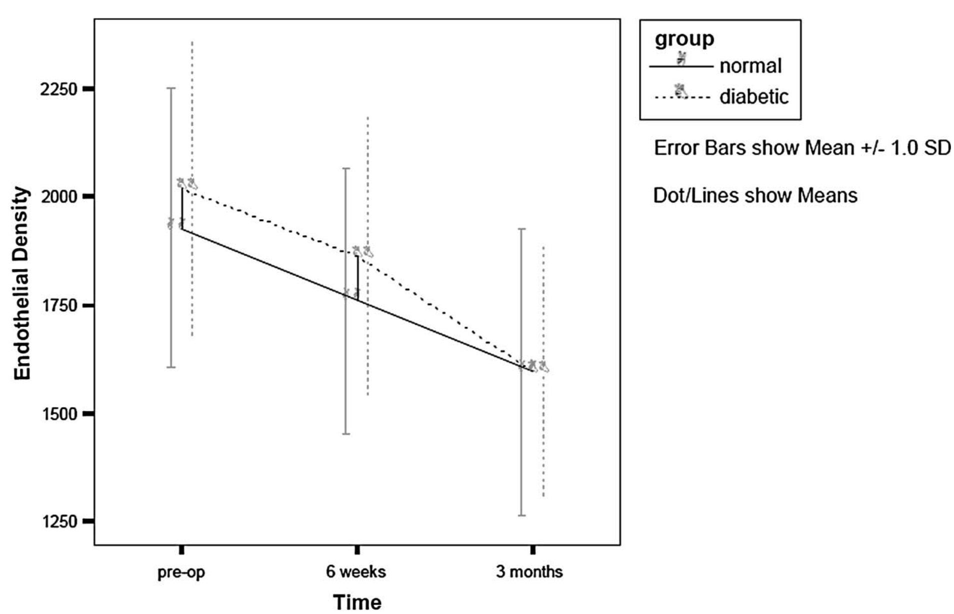

FIGURE 1. Pattern of change in the ED in patients with T2DM and normal individuals postoperatively.

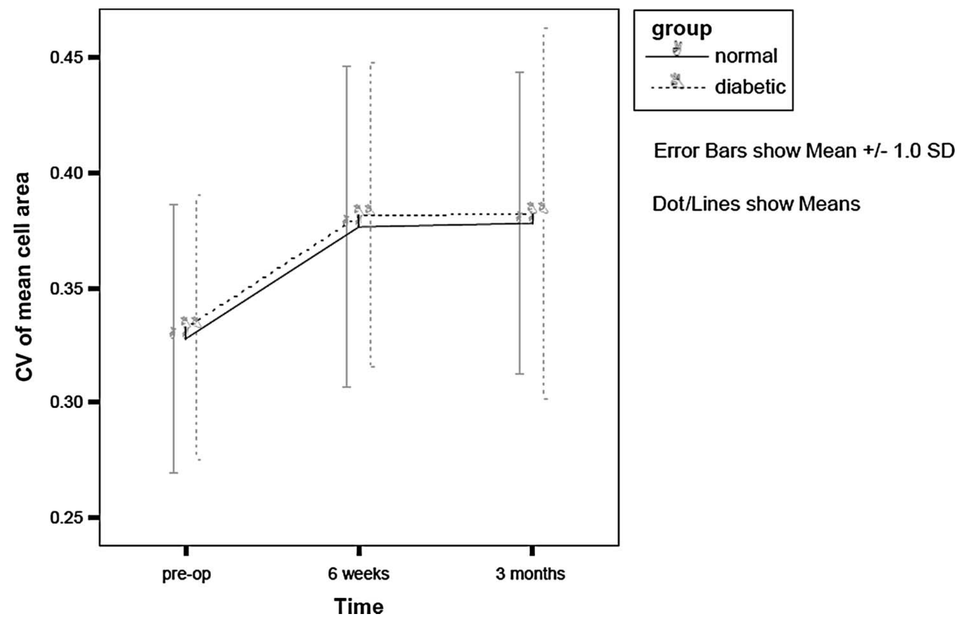

FIGURE 2. Patterns of change in CV in the 2 groups postoperatively.

done by Ventura et al[6] showed a significant endothelial loss with an increase in the CCT after cataract surgery, the latter returning to normal values within 3 months.

Our study did not show a significant difference in endothelial count in the different age groups. The preoperative ED was more present in patients with diabetes. An error of 10% may be accounted for the screening methods, and changes of less than 200 cells may be attributed to measurement variability, which could be instrument related.[14] The difference found in our study between patients with diabetes and normal individuals was less than 100 cells, which is an acceptable instrument-related error. The coefficient of variation was higher in patients with diabetes with no statistical significance. The maximum duration of diabetes in our study population was only 20 years, which might be the cause for the absence of morphological changes characteristically explained in patients with diabetes.[15] The CCT was found to be more in the patients with diabetes in our study, as described in literature,[16] with statistically significant difference from the normal patients. The ED was found to steadily decrease after cataract surgery in both the groups, with a significant difference in the percentage of endothelial loss between 6 weeks and 3 months, which was much more in patients with diabetes.

The CV, being an indicator of the repair process after endothelial loss, was found to have increased postoperatively in both the groups, reaching a steady state after 6 weeks, with the values being higher in the diabetic group. However, this difference was not statistically significant. The percentage of hexagonal cells could not be assessed in these eyes because our software did not have the facility for automated reading for the same. So, the failure to find an increase in the coefficient of variation in our study between 6 weeks and 3 months might be because of the drop in the percentage of hexagonal cells without change in the coefficient of variation in these eyes during the repair process. But previous studies have also failed to show a significant increase in the coefficient of variation postoperatively, despite the continued endothelial loss.[10] The CCT followed a pattern of maximum increase at the 2-week follow-up, with a slow reduction until the 3-month follow-up in both the groups. The CCT never returned to the preoperative value. This was in contrast to what is described in the

TABLE 3. Comparison of Change in CCT in Normal Individuals and Patients With T2DM Postoperatively

Status	CCT at 2 Weeks	CCT at 6 Weeks	CCT at 3 Months
Normal individuals (n = 165)	542 ± 33.6	526 ± 31.6	523 ± 33.0
Patients with T2DM (n = 158)	550 ± 33.0	533 ± 33.2	528 ± 30.0

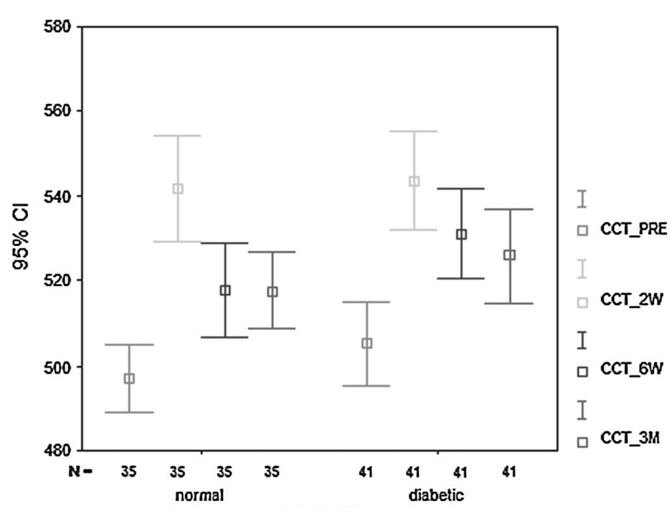

FIGURE 3. Comparison of pattern of change in the CCT in normal individuals and in patients with T2DM.

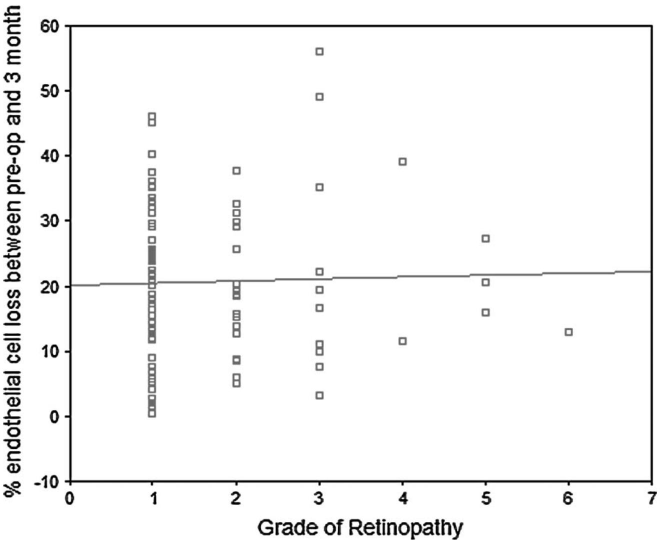

FIGURE 4. Correlation of grade of retinopathy with percentage of endothelial cell loss at 3 months postoperatively.

literature.[17] This difference may be because of the difference in surgical techniques used in the studies.

This study also looked at the risk factors in diabetes that can lead to increased endothelial cell loss. There was no significant difference in the endothelial cell loss among various grades of retinopathy, which is comparable to other studies done on patients with diabetes with and without retinopathy after planned ECCE.[18] There was no association between the endothelial cell loss and the HbA_1C levels. The percentage of endothelial cell loss was found to be more in patients who had longer duration of surgery. But the grade of cataract was found to have no association with endothelial loss postoperatively. This observation is against various studies that consider grade of nucleus as one of the most important risk factors for endothelial cell loss.[19] However,

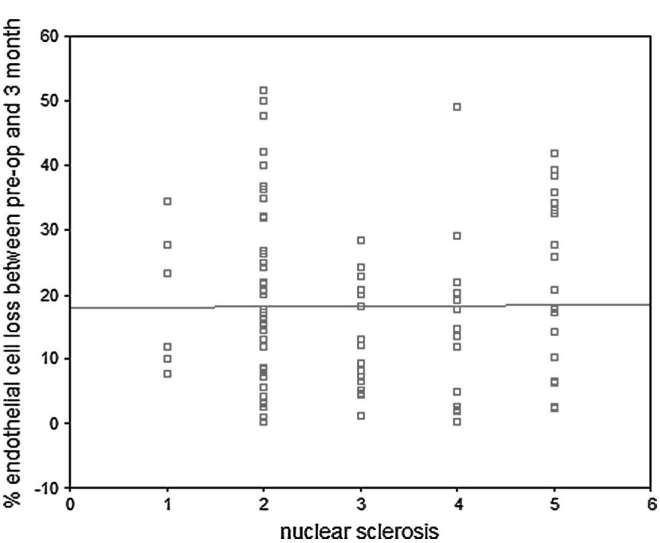

FIGURE 5. Correlation of grade of cataract with the percentage of endothelial cell loss at 3 months postoperatively.

TABLE 4. Correlation of Percentage of Endothelial Cell Loss With the Duration of the Surgery

Duration of Surgery (Min)	Percentage of Endothelial Cell Loss
15–30	15.27 ± 12.52
30–45	20.84 ± 14.25

because those studies were done in patients undergoing phacoemulsification, the increased ultrasound energy required for harder nuclei could have caused the endothelial damage. The limitations of this study were a short follow-up period, inadequacy of the specular microscope software to automatically calculate the percentage of hexagonal cells, the short duration (<20 years) of diabetes, lower grades of retinopathy, and fair glycemic control in the sample studied.

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