Comparison of corneal endothelial changes following phacoemulsification in diabetic and non-diabetic patients

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Purpose: To study corneal endothelial changes post phacoemulsification in diabetic and non-diabetic patients. **Methods:** A comparative, prospective, observational study was conducted on 100 diabetic and 100 non-diabetics who underwent phacoemulsification. All patients were operated by the same surgeon by using the phaco chop technique to exclude any surgeon-related bias. Endothelial cell count, CCT, and coefficient of variance (CV) were measured with a specular microscope along with BCVA preoperatively and at 1 week, 4 weeks, and 3 months postoperatively. For statistical analysis, data were analyzed by using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA). Data were summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Chi square test, independent sample T test, and paired T test were used to compare the data. $P \leq 0.05$ was considered statistically significant. **Results**: Postoperatively at 1 week, 4-week, and 3 months follow-up intervals, the mean endothelial cell count and coefficient of variance were significantly higher, and the mean percentage of hexagonal cells was significantly lower in non diabetic as compared to the diabetic group. A significant difference in mean central corneal thickness of the two groups was observed at 1-week and 4-weeks postoperative intervals; at both these intervals, the mean value was significantly higher in non diabetic as compared to the non-diabetic group. However, at 3-months post-operative interval, the difference between the two groups was not significant statistically. Mean BCVA values were significantly higher in diabetic as compared to the diabetic group at all three follow-up intervals. **Conclusion**: The findings of the present study show that endothelial cell characteristics are adversely affected in diabetic eyes as compared to non-diabetic patients undergoing phacoemulsification; this might also have an effect on the visual outcomes.

Key words: BCVA, central corneal thickness, corneal endothelium, diabetes, endothelial cell count, hexagonality, phacoemulsification

Cataract has been documented to be the number one cause of curable blindness globally[1] and remains the leading cause of blindness in India (62.60%).[2] Removal of the cloudy lens and implantation of a clear intraocular lens is the only definite treatment of cataract.[3] Phacoemulsification with foldable intra ocular lens implantation has become the gold standard treatment procedure for cataract management.[4,5]

The hexagonal cells of the endothelium of cornea are responsible for maintaining the clarity of the cornea by actively removing water. These cells have limited mitotic capacity, and any disturbance in the endothelial homeostasis might have a profound effect on the clarity of the cornea.[6]

The corneal endothelium is known to undergo damage during cataract surgery. Factors such as advanced age, increasing infusion volume, and increasing the amount of ultrasound energy and phaco time are the main risk factors for corneal endothelial damage.[7]

Diabetes mellitus is a major health concern in our modern-day lives,[8] affecting more than 415 million people worldwide (2015)[9] and causing neuropathies, nephropathies,

and CNS and eye complications. It can affect all structures of the eye, causing complications such as diabetic retinopathy, diabetic cataract, punctate epithelial keratopathy, recurrent corneal erosions, corneal edema, delayed wound healing, and persistent epithelial defects.[10,11]

The diabetic cornea, which is more fragile and vulnerable to trauma, possesses a weaker compensatory capacity. The corneal endothelium of a patient with diabetes mellitus has been shown to exhibit polymegathism and pleomorphism.[12,13] Although the cornea may appear disease free in the diabetics, an awareness of the marked biochemical and ultrastructural abnormalities in the diabetics can enable us to prevent more overt complications.[14]

Increasing age decreases the endothelial cell count, and most of the patients undergoing cataract surgery are usually elderly, which may have a negative impact on the surgical outcome.[15] This factor coupled with the effect of diabetes mellitus indicate

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a great risk of long-term endothelium cell dysfunction with decompensation and the development of bullous keratopathy.

The corneal endothelium is evaluated by central corneal thickness (CCT), corneal endothelial cell density (ED), and morphology pre and postoperatively.[16] Specular microscopy is a non-invasive and the most accurate photographic technique that can be used to visualize and analyze the corneal endothelium.[17]

Studies that have been carried out so far on the importance of corneal abnormalities commonly found in diabetic patients after cataract surgery due to factors including the diabetic state. Surgical procedures[18-22] yield conflicting results concerning the differences in corneal properties between diabetic and non-diabetic patients after phacoemulsification.

Thus, this study was carried out to assess the vulnerability of the corneal endothelium in diabetics and non-diabetics undergoing phacoemulsification to avoid postoperative corneal edema and improve the final visual outcome.

Methods

A 1-year comparative, prospective, observational study was carried out in the ophthalmology outpatient department in accordance with the tenets of the Declaration of Helsinki and was cleared by the institute's ethical committee.

The patients were divided into two groups: Diabetic: Patients diagnosed with type two diabetes mellitus with good glycemic control (HbA$_{1c}$ <7) and senile cataract. Serum glycosylated hemoglobin levels were obtained in all patients with diabetes to evaluate glycemic control. Non-diabetic: Age-matched patients without diabetes with senile cataract. Two random blood glucose tests were taken in accordance with recommendations of the American Diabetic Association to detect undiagnosed diabetes.

Patients in the age group of 40–60 years, willing to give informed consent for surgery and study and come for follow-up, with cataract grade of nuclear sclerotic cataract I to III, and with no history of previous ocular surgery were included in the study. Patients with a preoperative endothelial cell count of >1500 cells/mm^2 and an anterior chamber depth of >2.5 mm were included in the study. Patients with traumatic cataract, any corneal pathology (e.g., Fuch's dystrophy), pseudoexfoliation, history of ocular trauma or intraocular surgery, intraocular inflammation or any other ocular disease that may affect endothelial cell function (such as glaucoma, uveitis, patients with diabetic retinopathy or any other retinal pathology) were excluded from the study.

History of any eye disease, DM type and complications, onset age and duration, and blood glucose control method were recorded. All of the participants underwent a comprehensive eye examination. Visual acuity (VA) was recorded in both the eyes. Keratometry, A-scan, HbA1c levels in diabetic patients, and two random blood glucose levels in non-diabetic patients were recorded. Preoperative specular microscopy (Tomey, EM–1000, Japan) for evaluation of ED, coefficient of variation (CoV), CCT, and percentage of cell hexagonality (%Hex) was done. All patients were operated by a single well-experienced surgeon by using the same phacoemulsification equipment under topical anesthesia. The follow-up regimen was followed after 1 week,

1 month, and 3 months after cataract surgery. BCVA, slit-lamp examination, and specular evaluation of the endothelium was done on each follow-up.

The samples were calculated by assuming 80% power, 5% significance level with 95% confidence interval as well as absolute error being 44 and assumed standard deviation being 150. The total sample size calculated was 100 per group.

For statistical analysis, data were entered into a Microsoft Excel spreadsheet and then analyzed by using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA). Data were summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables.

Chi-square test, independent sample T test, and paired T test were used to compare the data. $P \leq 0.05$ was considered statistically significant.

Results

The present study was carried out to compare the corneal endothelial changes after phacoemulsification in diabetic and non-diabetic patients. For this purpose, a prospective, comparative, observational study was carried out that included a total of 200 patients scheduled to undergo phacoemulsification. Table 1 shows the group-wise distribution of cases, and Table 2 shows the diabetic profile of patients in the diabetic group.

Out of the total of 200 subjects enrolled in the study, a total of 100 subjects were diabetics with good glycemic control (HbA$_{1c}$ <7), whereas the remaining 100 were age-matched non-diabetics with senile cataract. The difference between the mean pre-op BCVA, IOP, and RBS values in non-diabetic and diabetic subjects was not significant for mean BCVA and IOP values ($P > 0.05$); however, mean RBS was significantly higher in diabetic as compared to the non-diabetic group ($P < 0.001$). The average cumulated dissipated phaco energy was statistically insignificant.

Statistically, there was no significant difference between mean ED in non-diabetic and diabetic groups preoperatively ($P = 0.091$). Postoperatively, mean values were higher in non-diabetic as compared to the diabetic group, and the difference between the two groups was significant statistically ($P < 0.001$) [Table 3]. With respect to intragroup comparisons, in both groups, the change from baseline was significant at all time intervals ($P < 0.001$). It was seen that the mean decline showed a gradual increase at each follow-up with maximum change observed at 3 months [Table 4].

Preoperatively, there was no significant difference in CoV between diabetics and non-diabetics ($P = 0.129$). Postoperatively, the mean CoV values were lower in non-diabetic as compared to the diabetic group, and the difference between the two groups was significant statistically at 1-week and 4-weeks post-operative intervals ($P < 0.001$). Values were higher in the diabetic group as compared to the non-diabetic group at 3-months too, but the difference was not found to be significant statistically ($P = 0.066$) [Table 3]. With respect to intragroup changes, in both the diabetic and non-diabetic groups, at all the time intervals, the change from baseline was significant statistically ($P < 0.001$). In both the groups, the peak change was at 4-week while the minimum change was at 3-months [Table 4].

Preoperatively, there was no significant difference in mean percentage hexagonal cell values between the two

Table 1: Comparison of the demographic profiles and baseline characteristics of the study population

Characteristic	Non-diabetic (*n*=100)	Diabetic (*n*=100)	Statistical significance, *P*
Mean age±SD (Range) in years	57.94±6.65 (43-70)	58.52±6.29 (45-69)	0.527
Gender			
Male	54	54	1.000
Female	46	46	
Side involved			
Left	46	39	0.317
Right	54	61	
Cataract grade			
I	14	14	0.311
II	51	41	
III	35	45	
Mean BCVA±SD (LogMAR)	0.67±0.20	0.69±0.21	0.519
Mean IOP±SD (mm Hg)	13.51±2.41	13.47±2.68	0.912
Mean RBS±SD (mg/dl)	122.74±11.34	131.18±17.75	<0.001

Table 2: Diabetic profile of patients in the diabetic group

Characteristic	Statistic
Mean duration of diabetes±SD (Range) in years	3.06±1.54 (1-8)
Mean HbA$_{1c}$±SD (Range) in %	6.12±0.38 (5.40-6.90)

groups (*P* = 0.274). Postoperatively, the mean values were higher in non-diabetic as compared to the diabetic group, and the difference between the two groups was significant statistically (*P* < 0.001) [Table 3]. With respect to intragroup comparison from baseline hexagonality, a significant change from baseline was observed in both the groups at all the follow-up intervals. In the non-diabetic group, the mean change from baseline was −6.74%, −4.47%, and −1.91%, respectively, at 1-week, 4-weeks, and 3-months intervals, thereby showing that with passage of time difference from baseline was diminishing. Similar trend were also observed in diabetic patients, though the difference from baseline was higher as compared to non-diabetic patients. In diabetic patients, the mean change from baseline was −12.89%, −9.60%, and −6.85% at 1-week, 4-weeks, and 3-months intervals, respectively (*P* < 0.001) [Table 4].

Preoperatively, there was no significant difference in CCT between the two groups (*P* = 0.330). At 1-week and 4-week follow-up intervals, the mean value was significantly higher in diabetic as compared to the non-diabetic group (*P* < 0.05). At 3-months, the mean value was higher in diabetic as compared to the non-diabetic group, but the difference between the two groups was not significant statistically (*P* = 0.745) [Table 3]. With respect to intragroup comparison, both the groups showed an increase from baseline at all the follow-up intervals. In the non-diabetic group, values at all three follow-up intervals was significantly higher as compared to baseline whereas in the diabetic group; the difference from baseline was significant statistically only at 1-week and 4-weeks postoperative intervals (*P* < 0.001) [Table 4].

Preoperatively, mean BCVA showed no significant difference between the two groups (*P* = 0.519). At 1-week, 4-weeks, and 3-months follow-up, the difference in BCVA between the two groups was found to be significant at all three follow-up intervals (*P* < 0.05) [Table 5].

Pearson correlation studies to find the relationship between the energy used during phacoemulsification and the various endothelial parameters did not show a significant correlation in diabetics and non-diabetic groups.

Discussion

In the present study, as compared to baseline, the mean changes in the endothelial cell density at first, second, and third follow-up intervals in the non-diabetic patients were significant statistically. In the corresponding time intervals, there was a mean change in the endothelial cell density at first, second, and third follow-up intervals in the diabetic group with a significant change from baseline from the first follow-up itself. It was seen that at all the follow-up intervals, the mean endothelial cell density in diabetic cases was significantly lower as compared to non-diabetic patients. In effect, the findings of the study showed that while cases experienced a marginal loss in endothelial cell density in non-diabetic population, the diabetic population showed a relatively much higher endothelial cell density loss.

Compared to the present study, Fernández-Muñoz[23] did not find a significant difference in the mean endothelial cell count between diabetic and non-diabetic patients. Contrary to these findings, in the present study, we found the mean count to be significantly lower in diabetic as compared to non-diabetic patients at all three follow-up intervals. The results in present study are somewhat close to the observations made by Al-Sharkawy *et al.*[24] who observed a % endothelial cell loss of 5.4% and 8.1%, respectively, at 1 month and 3-month follow-up intervals in diabetic patients and 6.5% and 8.4%, respectively, in the non-diabetic group. In a meta-analysis of 13 studies, Tang *et al.*[14] reported that diabetic patients tend to have a lower cell density as compared to non-diabetic patients; however, the extent of this difference is highly variable too.

In the present study, the mean CoV was higher in diabetic patients as compared to non-diabetic patients at all three follow-up intervals and the difference was significant statistically at 1-week and 4-weeks follow-up. In both groups, the change from baseline was significant statistically at all three

Table 3: Summary of corneal endothelial parameters preoperative and 1 week, 1 month, and 3-month post-op

Corneal parameters	Time interval	Group	Mean	SD	Minimum	Maximum	P
ECD	Pre-op.	Non-diabetic	2475.15	181.61	2116	3271	0.091
		Diabetic	2430.93	186.56	2100	2967	
	1-week post-op.	Non-diabetic	2403.22	190.72	1921	3068	<0.001
		Diabetic	2267.50	168.24	1982	2774	
	4-weeks post-op.	Non-diabetic	2371.55	193.18	1926	3042	<0.001
		Diabetic	2213.84	177.00	1923	2768	
	3-months post-op.	Non-diabetic	2323.95	195.00	1895	2989	<0.001
		Diabetic	2139.88	190.70	1734	2697	
CoV	Pre-op.	Non-diabetic	33.05	2.71	26	39	0.129
		Diabetic	33.68	3.11	26	39	
	1-week post-op.	Non-diabetic	37.76	3.23	30	43	<0.001
		Diabetic	39.89	3.24	32	46	
	4-weeks post-op.	Non-diabetic	38.14	3.58	30	43	<0.001
		Diabetic	40.25	3.26	32	48	
	3-months post-op.	Non-diabetic	35.13	4.73	25	46	0.066
		Diabetic	36.23	3.61	28	44	
% Hexagonal Cells	Pre-op.	Non-diabetic	73.90	3.24	66.00	80.00	0.274
		Diabetic	73.32	4.18	63.00	80.00	
	1-week post-op.	Non-diabetic	68.92	3.64	61.00	77.00	<0.001
		Diabetic	63.87	4.05	54.00	76.00	
	4-weeks post-op.	Non-diabetic	70.60	3.94	61.00	81.00	<0.001
		Diabetic	66.28	4.08	57.00	78.00	
	3-months post-op.	Non-diabetic	72.49	4.08	62.00	85.00	<0.001
		Diabetic	68.30	4.24	59.00	81.00	
CCT	Pre-op.	Non-diabetic	518.29	15.82	483	576	0.330
		Diabetic	520.46	15.59	469	554	
	1-week post-op.	Non-diabetic	527.73	13.40	495	564	<0.001
		Diabetic	536.25	16.72	492	579	
	4-weeks post-op.	Non-diabetic	523.85	13.90	491	570	0.003
		Diabetic	530.20	15.67	479	567	
	3-months post-op.	Non-diabetic	522.42	12.70	490	557	0.745
		Diabetic	523.71	17.70	466	560	

Table 4: Evaluation of intragroup change in cell-density, CoV, CCT, and hexagonality at different follow-up intervals as compared to baseline

Corneal Parameters	Comparison	Non-diabetic Group				Diabetic group			
		Change from baseline			P (Paired t-test)	Change from baseline			P (Paired t-test)
		Mean	SD	%		Mean	SD	%	
Change in Endothelial cell density	Baseline vs. 1-week	-71.93	180.89	−2.91	<0.001	-163.43	71.61	−6.72	<0.001
	Baseline vs. 4-weeks	-103.60	184.45	−4.19	<0.001	-217.09	84.37	−8.93	<0.001
	Baseline vs. 3-months	-151.20	178.41	−6.11	<0.001	-291.05	95.25	−12.0	<0.001
Change in Coefficient of Variance (CoV) (%)	Baseline vs. 1-week	4.71	4.67	14.25	<0.001	6.21	2.27	18.44	<0.001
	Baseline vs. 4-weeks	5.09	4.93	15.40	<0.001	6.57	2.27	19.51	<0.001
	Baseline vs. 3-months	2.08	5.85	6.29	0.001	2.55	2.61	7.57	<0.001
Change in hexagonal cellularity	Baseline vs. 1-week	−4.98	3.46	-6.74	<0.001	−9.45	5.02	−12.89	<0.001
	Baseline vs. 4-weeks	−3.30	4.11	−4.47	<0.001	−7.04	4.74	−9.60	<0.001
	Baseline vs. 3-months	−1.41	4.02	-1.91	0.001	−5.02	4.79	−6.85	<0.001
Change in CCT	Baseline vs. 1-week	9.44	5.25	1.82	<0.001	15.79	7.53	3.03	<0.001
	Baseline vs. 4-weeks	5.56	4.44	1.07	<0.001	9.74	6.24	1.87	<0.001
	Baseline vs. 3-months	5.13	15.01	0.99	0.001	2.25	13.84	0.43	0.107

Table 5: Comparison of mean BCVA (LogMAR) at preoperative and different postoperative follow-up intervals between non-diabetic and diabetic groups

Time interval	Group	n	Mean	SD	Minimum	Maximum	Median	P
Pre-op.	Non-diabetic	100	0.67	0.20	0.30	1.00	0.60	0.519
	Diabetic	100	0.69	0.21	0.30	1.00	0.60	
1-week post-op.	Non-diabetic	100	0.15	0.10	0.10	0.30	0.20	0.034
	Diabetic	100	0.18	0.09	0.10	0.30	0.20	
4-weeks post-op.	Non-diabetic	100	0.005	0.02	0.00	0.1	0.00	0.001
	Diabetic	100	0.02	0.02	0.00	0.1	0.00	
3-months post-op.	Non-diabetic	100	0.003	0.02	0.00	0.10	0.00	0.005
	Diabetic	100	0.014	0.03	0.00	0.10	0.00	

follow-up intervals. The trends show that there was a rise in CoV during the initial postoperative period; however, it tended to reduce over time. The findings clearly show that the impact of cataract surgery on CoV was much pronounced in diabetic as compared to the non-diabetic group. Morikubo et al.[6] and Yan et al.[25] in their studies found below baseline values at follow-up in diabetic patients, thus showing a mean fall in CoV rather than an increase. In the meta-analysis of 13 studies, Tang et al.[15] found that at 3-months post-operative interval, the mean difference in CoV of diabetic and non-diabetic groups was 6.65%, with mean values higher in diabetic as compared to non-diabetic patients.

In the present study, we found the mean % hexagonal cells to be significantly lower in diabetic as compared to the non-diabetic group at all three follow-up intervals. In both groups, the mean values at different follow-ups were significantly lower as compared to baseline values. Pandey et al.[26] did not find a significant difference in % hexagonal cells between diabetic and non-diabetic groups at 4-weeks interval but found a significant difference between the two groups with lower mean values in diabetic as compared to non-diabetic group at 1-week and 3-months intervals. Different trends of change in hexagonal cells in different studies highlight the need to device a more objective criteria for hexagonal cell density evaluation in view of the subjective observation dependence. Nevertheless, given the observations being done by the same observer for both groups, the present study as well as all the previous studies found hexagonality to be significantly higher in non-diabetic as compared to the diabetic group. Other studies also find that at a given time, hexagonality was higher in non-diabetic as compared to diabetic patients.

In the present study, the mean central corneal thickness was seen to be significantly higher in diabetic as compared to non-diabetic group at 1-week and 4-weeks follow-up intervals. At 3-months follow-up, the mean value was higher in diabetic patients as compared to non-diabetic patients (~0.8 μm), but the difference between the two groups was not significant statistically. With respect to intragroup changes, in both groups, there was an increase in CCT at different follow-up intervals as compared to baseline, though in percentage terms this change was nominal. Compared to the present study, Kudva et al.[27] found CCT of diabetic patients to be significantly higher as compared to non-diabetic patients at both 1-month as well as 3-month intervals. The reason for the higher difference in CCT of diabetic and non-diabetic patients in their study as compared to the present study could be attributable primarily to the fact

that in the present study, all the diabetics had an excellent glycemic control (HbA$_{1c}$ values ranging from 5.40% to 6.90%; mean value: 6.12 ± 0.38%), whereas Kudva et al.[27] reported the mean HbA$_{1c}$ value of 7.56%, thus indicating poor glycemic control as compared to that in the present study. In fact, the better glycemic control of patients in the present study was one of the reasons for difference in some of the specific trends of changes in endothelial cell density and CCT observed in present study as compared to those reported in the literature. In fact, in such a highly controlled glycemia, the diabetic patients in the present study were too close to non-diabetic patients as hyperglycemia is considered to be one of the major factor responsible for greater cellular damage and delayed tissue regeneration. In their meta-analysis, Tang et al.[15] also observed no significant difference in mean change in CCT of diabetic and non-diabetic patients at 1- week and 3-months follow-up; however, at the 1-month interval, the mean changes were significantly higher in diabetic as compared to non-diabetic group. In fact, almost all the studies including ours have seen that impact of cataract surgery on central corneal thickness is nominal and is almost neutralized by 3-months postoperative period.

In the present study, we included visual outcomes in terms of postoperative visual acuity and found that non-diabetic patients had significantly better visual outcomes as compared to diabetic patients at all three follow-up intervals. In their meta-analysis, Tang et al.[15] also found short-term visual acuity (1 week) to be better in non-diabetic as compared to a diabetic group; however, they did not find it to be maintainable up to 3-months follow-up. As such visual outcome measure is one of the less-studied outcomes in studies evaluating the endothelial cell changes following cataract surgery as most of the cases have a near-perfect vision in the affected eye during this short period, further studies to evaluate these changes in long-term are recommended to elucidate further on this aspect.

The findings of the present study could be specific in view of the good glycemic control of diabetic patients and that peculiarity makes it different from other studies. The present study shows that though in the short term endothelial cell damage is higher in diabetic as compared to non-diabetic cases, with the passage of time despite slower repair in diabetic as compared to non-diabetic patients, these differences tend to neutralize. Further studies on a wider glycemic control profile of diabetic patients and their comparison with non-diabetic patients in a study with longer follow-up are recommended to explore this association further.

Conclusion

The present study was carried out to compare the corneal endothelial changes after phacoemulsification in diabetic and non-diabetic patients. Postoperatively at 1 week, 4-week, and 1-month follow-up intervals, the mean endothelial cell count and coefficient of variance were significantly higher, and the mean % of hexagonal cells was significantly lower in diabetic as compared to the non-diabetic group. A significant difference in the mean central corneal thickness of the two groups was observed at 1-week and 4-weeks postoperative intervals. At both these intervals, the mean value was significantly higher in diabetic as compared to the non-diabetic group. However, at 3-months postoperative interval, the difference between the two groups was not significant statistically. Mean BCVA values were significantly higher in diabetic as compared to the non-diabetic group at all three follow-up intervals.

The findings of the present study show that endothelial cell characteristics are adversely affected in diabetic as compared to non-diabetic patients, which might also have an effect on the visual outcomes. The findings of the present study are in agreement with the findings of previous works. However, whether these differences sustain in the long-term needs further studies in a long-term longitudinal cohort study.

Conflicts of interest

There are no conflicts of interest.

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