

Comparison of Corneal Endothelial Cell Counts in Patients with Controlled Diabetes Mellitus (Type 2) and Non Diabetics after Phacoemulsification and Intraocular Lens Implantation

Dr. Akram Khan^{1§}, Dr. Sanhita Kose², Dr. M.K.Jharwal³, Dr. Anju Meena⁴ and Dr. Arun Sharma⁵

Upgraded Department of Ophthalmology, SMS Medical College, Jaipur, Rajasthan

Abstract—Cataract is the main cause of blinding and Diabetes Mellitus (DM) is the one of major cause of early cataract. Patients of DM has poor So this study is aimed to assess the corneal endothelial cell count in patients of DM (Type 2) after phacoemulsification and intra-ocular lens implantation. This study was conducted on 66 patients of cataract, out of which 33 patients with and 33 without DM (Type 2). Both groups underwent pre operative investigation and ophthalmological assessment and then undergo phacoemulsification done by same surgeon. After phacoemulsification all cases were followed up on 1st day, 1st week, 1 month and 3 months and Uncorrected visual acuity (UCVA), Best corrected visual acuity (BCVA), corneal thickness, endothelial cell count and morphometric analysis were recorded. Both groups parameters were compared with unpaired 't' test. At the end of 3 months it was found that the mean endothelial cell loss in Group A (Diabetic) was $6.9\% \pm 0.6$ and in Group B (control) was $2.4\% \pm 0.3$ suggesting that the corneal endothelium in diabetic patients is under metabolic stress, and weaker against mechanical loads, such as phacoemulsification, than that in non-diabetic subjects. Despite good glycemic control and no corneal abnormalities before surgery. Endothelium in diabetic subjects is more vulnerable to surgical trauma and has a lower capability in the process of repair. These findings should be considered when planning cataract surgery in patients with diabetes.

Keywords: Diabetes Mellitus Type 2, Glycemic Control, Corneal Endothelial Cells, Phacoemulsification, Cell Repair.

I. INTRODUCTION

Sight is one of the best and most precious gifts that god has bestowed upon us. Out of all the blinding diseases in our country, cataract has been documented to be the most significant cause of bilateral blindness. In India cataract has been reported to be responsible for 50-80% of the bilaterally blind in the country.^{1,2} Worldwide more than 285 million people are affected by diabetes mellitus. This number is expected to increase to 439 million by 2030 according to the International Diabetes Federation.³

Phacoemulsification is nowadays the preferred technique for most types of cataract due to less astigmatism, less post operative inflammation and rapid visual recovery.

With specular microscope, it has been detected that normal endothelial cell count is approximately 3400 cells/mm² in children decreasing to 2500 cells/mm² in old age with increased polymegathism and pleomorphism.^{4,5}

Corneal endothelial cell loss has been documented as one of the complications of phacoemulsification surgery. In the vast majority of conditions that produce corneal edema, it is the endothelial layer that is malfunctioning – an observation which ensures that ophthalmic surgeon shows due respect to this layer and evaluate it accordingly.

In diabetes, raised blood glucose levels causes transformation of glucose into sugar alcohol which accumulates in cells. Aldose reductase in polyol pathway is disturbed over corneal epithelial and endothelial cells, while accumulation of sugar alcohol leads to increased osmotic pressure, rendering corneal endothelial cells more vulnerable. It has been suggested that high levels of glucose reduce corneas ability to control hydration/dehydration and impairs the activity of the $\text{Na}^+ - \text{K}^+$ ATPase enzyme in corneal endothelial cells and interferes with the functions of this fluid pump. Such metabolic stress evidently impairs the ability of corneal endothelial cells to resist mechanical stress such as phacoemulsification.

So this case-control study is aimed to assess the corneal endothelial cell count in patients of DM (Type 2) after phacoemulsification and intra-ocular lens implantation.

II. METHODOLOGY

The study was conducted in Upgraded Department of Ophthalmology, S.M.S. Medical College and Hospital, Jaipur. Total 66 cataract patients were included in this study, out of which 33 patients with and 33 patients without DM (Type 2) were there. Both groups underwent pre operative investigation and ophthalmological assessment and then undergo phacoemulsification with IOL implantation by same surgeon after taking written informed consent.

Group A – Patients with controlled diabetes mellitus type 2 (33 eyes of 33 patients) who underwent phacoemulsification and IOL implantation.

Group B – Non diabetic patients (33 eyes of 33 patients) who underwent phacoemulsification and IOL implantation.

Criteria of inclusion were Senile uncomplicated cataract (Age range between 45 years to 75 years), Cataracts grade 1-2, Duration of diabetes > 5yrs, Normal fundus examination (No evidence of diabetic retinopathy), Endothelial cell count (ECC) of atleast 2000 per mm^2 .

Criteria of exclusion were any Corneal pathology, History of ocular trauma/intra-ocular surgery/Lasik, Ocular inflammation, Pre-operative endothelial count <2000 per mm^2 , Pre-operative anterior chamber depth <2.5mm, Age < 45yrs, Duration of diabetes < 5yrs, Cataract grade 3-4 (Hard Cataracts), Pseudoexfoliation, Preexisting posterior segment pathology (Retinal detachment, Vitreous haemorrhage).

Preoperatively, all patients underwent a slit-lamp and fundus examination, measurements of uncorrected and best-corrected visual acuity and intraocular pressure (IOP), keratometry, A scan and IOL power calculation. The central endothelial cell density (cells per square millimeter), variation in size of endothelial cells (CV), percentage of hexagonal cells, and Central corneal thickness (CCT) were analyzed using a noncontact specular microscope.

Preoperative investigations done are Blood sugar Fasting or Random, HbA1c levels in diabetic patients, Urine complete, ECG, Blood pressure.

Preoperative medication-Ciprofloxacin eye drops 2 hourly one day prior to surgery in the eye to be operated, Tab. Ciprofloxacin 500 mg B.D. for 1 days

Surgical Technique: All surgeries were performed by the same surgeon under topical anaesthesia using proparacaine 0.5% eye drops after pupillary dilation with tropicamide 0.8% and phenylephrine 5% eye

drops/Flurbiprofen eye drop, The surgical technique was very similar in all cases following a standardized procedure: sterile drape, speculum, topical anesthesia on the cornea (proparacaine 0.5%), single 0.9 mm side port was created, dye injected in Anterior Chamber (AC) and was formed with ophthalmic viscoelastic device (OVD), biplanar clear corneal incision was created superotemporally using a 2.8 mm keratome, capsulorrhexis done followed by hydrodissection/hydrodelineation, phacoemulsification performed with kelman-type microtip (30 degree), irrigation/aspiration (I/A) done and after filling the AC with OVD, foldable IOL with the recommended injector system was implanted into the eye. Finally OVD was removed with the I/A tip and the stromal wound was hydrated. Surgery time was recorded starting from creating the side port to the end of stromal wound hydration. The effective phacoemulsification time (EPT) was recorded.

Postoperative Medication: Tobramycin 0.3%+Dexamethasone 0.1% eye drops 2 hourly for 1 weeks followed by tapering dose, Tropicamide 0.8% eye drop once during night time.

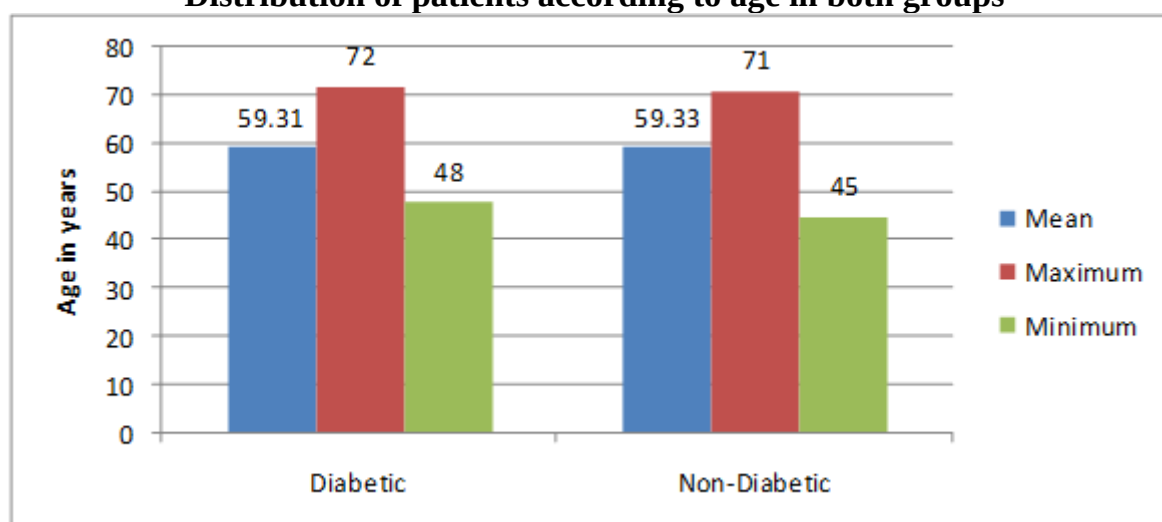
Follow Up: The follow up examination was conducted 1 day, 1 week, 1 month and 3 months postoperatively. During follow up, patients were assessed for: Endothelial Cell count, Morphometric analysis using Specular Microscope, Visual acuity-UCVA and BCVA was measured.

Statistical Analysis: Statistical analysis was done using paired t test to compare preoperative and postoperative data and unpaired t test to compare results between the two groups

III. RESULTS

Sixty six eyes of 66 cataract patients were enrolled, out of which in group 'A' 33 patents with DM type 2 and in Group 'B' 33 patients without DM Type 2. Age and sex wise distribution of both the group were well comparable ($p > 0.05$). Mean age in group 'A' was 59.31 ± 6.2 years and in group 'B' was 59.33 ± 8.8 years ($p = 0.98$). (Figure 1)

Figure 1
Distribution of patients according to age in both groups



Mean Endothelial Cell Counts (ECC) in Group A, preoperatively was $2784.1 \pm 244/\text{mm}^2$ and in Group B, was $2655.2 \pm 302.1/\text{mm}^2$ ($P = 0.05$). This difference was not found significant. (Table 1)

Post-operatively, mean endothelial cell count dropped to 2622.8 ± 239.4 on 1st post operative day, 2606.1 ± 244.0 at 1 week, 2598.1 ± 244 at 1 month and 2592.1 ± 244.0 at 3 months in group A. This variation was found significant. (Table 1)

In Group B, the mean Endothelial Cell Counts (ECC) dropped to $2610.8 \pm 302.0/\text{mm}^2$ on 1st post-operative day, $2599.8 \pm 302.5/\text{mm}^2$ at 1 week, $2594.3 \pm 302.1/\text{mm}^2$ at 1 month and $2591.3 \pm 302.1/\text{mm}^2$ at 3 months. This variation was found not significant. (Table 1)

Table 1
Comparison of Cell Counts in Both 'A' and 'B' Group

S. No.	Cell Counts Variable	Diabetic Gp 'A'	Non DM Gp 'B'	*P Value	LS
1	Pre-operative	2784 (244)	2655(302)	0.061	NS
2	1 Day Post operative	2622 (239.4)	2610.8 (302)	0.988	NS
3	1 Week Post operative	2606.1 (244)	2599.8 (302.5)	0.930	NS
4	1Month Post operative	2598.1 (244)	2594.3 (302.1)	0.953	NS
5	3 Months Post operative	2592.1 (244)	2591.3 (302)	0.988	NS
	P Value (by ANOVA) LS	0.006 S	0.912 NS		

*** Unpaired 't' Test at 64 DF**

The mean Coefficient of Variance (CV) in group A was 34.25 ± 4.4 and in group B was 34.06 ± 4.6 . There was no statistically significant ($p=0.86$) difference between the two. Postoperatively, the mean CV on 1st day, at 1 week, 1 month and 3months was 36.24 ± 4.5 , 37.09 ± 4.6 , 37.55 ± 4.7 and 37.69 ± 4.7 in group A and 36.08 ± 5.0 , 37.05 ± 5.4 , 37.48 ± 5.5 and 37.51 ± 5.5 in group B. Although within the group these variations were with significant difference but the difference in the mean CV between the two groups was not significant statistically. (Table 2)

Table 2
Comparison of Mean Coefficient of Variance (CV) in Both 'A' and 'B' Group

S. No.	Coefficient of Variance	Diabetic Gp 'A'	Non DM Gp 'B'	*P Value	LS
1	Pre-operative	34.25 ± 4.4	34.06 ± 4.6	0.864	NS
2	1 Day Post operative	36.24 ± 4.5	36.08 ± 5.0	0.892	NS
3	1 Week Post operative	37.09 ± 4.6	37.05 ± 5.4	0.974	NS
4	1Month Post operative	37.55 ± 4.7	37.48 ± 5.5	0.956	NS
5	3 Months Post operative	37.69 ± 4.7	37.51 ± 5.5	0.887	NS
	P Value (by ANOVA) LS	0.016 S	0.041 S		

*** Unpaired 't' Test at 64 DF**

After the surgery the mean percentage of hexagonality dropped in both the groups. In group A it reduced to 55.5 ± 5.2 on 1st post-operative day, 52.9 ± 5.6 at 1 week, 50.4 ± 5.4 at 1 month and 49.3 ± 5.5 at 3 month. In group B it reduced to 58.5 ± 6.3 on 1st day, 57.1 ± 6.7 at 1 week, 56.9 ± 6.0 at 1 month and 56.8 ± 6.5 at 3 months. (Table 3)

Though the mean percentage of hexagonality gradually significantly decreased in both the groups, but this decrease was significantly more in non-diabetic group. (Table 3)

Table 3
Comparison of Hexagonal cell Counts in Both 'A' and 'B' Group

S. No.	Hexagonal cell Counts	Diabetic Gp 'A'	Non DM Gp 'B'	*P Value	LS
1	Pre-operative	58.9±4.8	61.2±5.4	0.072	NS
2	1 Day Post operative	55.5±5.2	58.5±6.3	0.039	S
3	1 Week Post operative	52.9 ±5.6	57.1±6.7	0.007	S
4	1Month Post operative	50.4±5.4	56.9±6.0	<0.001	S
5	3 Months Post operative	49.3±5.5	56.8±6.5	<0.001	S
	P Value (by ANOVA) LS	<0.001 S	0.021 S		

***Unpaired 't' Test at 64 DF**

Good, fast and stable visual rehabilitation is the goal of cataract surgery and Visual Acuity is one of the best parameters to evaluate the quality and efficiency of a surgical technique. In this study, there was no significant difference in the Uncorrected Visual Acuity (UCVA) and Best corrected Visual Acuity (BCVA) between the two groups. (Table 4)

UCVA in group A was 0.67±0.1 and in group B was 0.66±0.1 which was not found significantly (P = 0.686) different. BCVA in group A was 0.28±0.1 and 0.25±0.1 in group B which was not found significantly (P = 0.227) different. (Table 4)

Post-operatively on 1st day the UCVA in group A was 0.29±0.1 and 0.26±0.1 in group B. It was found was significantly increased in both the groups (P < 0.001) but the difference between the groups was not statistically significant. (Table 4)

Likewise post operative BCVA was 0.16±0.1 in group A and 0.11±0.1 in group B. It was significantly increased in both the groups (P < 0.001) and it was significantly higher in group B as compared to group A. (Table 4)

Table 4
Comparison of Visual Acuity in Both 'A' and 'B' Group

S. No.	Visual Acuity	Hexagonal cell Counts	Diabetic Gp 'A'	Non DM Gp 'B'	*PValue	LS
1	UCVA	Pre-operative	0.67±0.1	0.66±0.1	0.686	NS
2		1 Day Post operative	0.29±0.1	0.26±0.1	0.227	NS
	P Value (by Paired 't' Test) LS		<0.001 S	<0.001 S		
1	BCVA	Pre-operative	0.28±0.1	0.25±0.1	0.227	NS
2		1 Day Post operative	0.16±0.1	0.11±0.1	0.046	S
	P Value (by Paired 't' Test) LS		<0.001 S	<0.001 S		

*** Unpaired't' Test at 64 DF**

There was no significant preoperative difference in endothelial cell density, cell size and hexagonal cell counts in both Diabetic and Non-Diabetic group. So both group were comparable on the basis of endothelial cell density, cell size and hexagonal cell counts. (Table 5)

Table 5
Comparison of Studied Parameters in Both 'A' and 'B' Group

S. No.	Variables	Diabetic Gp 'A'	Non DM Gp 'B'	* Test	P Value	LS
1	Cell Density in Cells/mm² (SD)					
	Pre-operative	2784 (244)	2655(302)	1.909	0.061	NS
	Post operative	2592 (244)	2591(302)	0.015	0.988	NS
	Difference in Pre and post operative	192	64			
	% of Difference	6.9 % (0.6)	2.4 % (0.3)	38.536	<0.001	S
2	Cell Size in mm³ (SD)					
	Pre-operative	34.3 (4.4)	34.1 (4.6)	0.180	0.857	NS
	Post operative	37.7 (4.7)	37.5 (5.5)	0.159	0.874	NS
	Difference in Pre and post operative	3.4	3.4			
3	Hexagonal Cells in % Cells/mm² (SD)					
	Pre-operative	58.9 (4.8)	61.2 (5.4)	-1.829	0.072	NS
	Post operative	49.3 (5.5)	56.8 (6.5)	-5.061	<0.001	S
	Difference in Pre and post operative	-9.6	-4.4			

*** Unpaired 't' Test at 64 DF**

When both the group i.e. Diabetic and Non-Diabetic were compare together, it was found that although post operative comparison of cell count showed no significant difference in both the group but when percentage of difference of pre to post operative cell counts were compare, it was found significantly ($p < 0.001$) more in diabetic group than non diabetic group. (Table 5)

Likewise when both the group in Diabetic and Non-Diabetic were compare together as per cell size, it was found that pre-operatively as well as post operatively cell size was without significant difference ($p > 0.05$). (Table 5)

When both the group i.e. Diabetic and Non-Diabetic were compare together as per Hexagonal cell counts, it was found that it was significantly ($p < 0.001$) less in diabetic group than non diabetic group. (Table 5)

These two groups were compared after complete 3-month follow-up. At the end of 3 months we found that the mean endothelial cell loss in Group A (Diabetic) was $6.9\% \pm 0.6$ and in Group B (control) was $2.4\% \pm 0.3$ suggesting that the corneal endothelium in diabetic patients is under metabolic stress, and weaker against mechanical loads, such as phacoemulsification, than that in non diabetic subjects. (Figure 2 & 3).

Figure 2
Specular microscopy in a Patient with Diabetes.
Image A= Pre-Operative and Image B = Post-operative

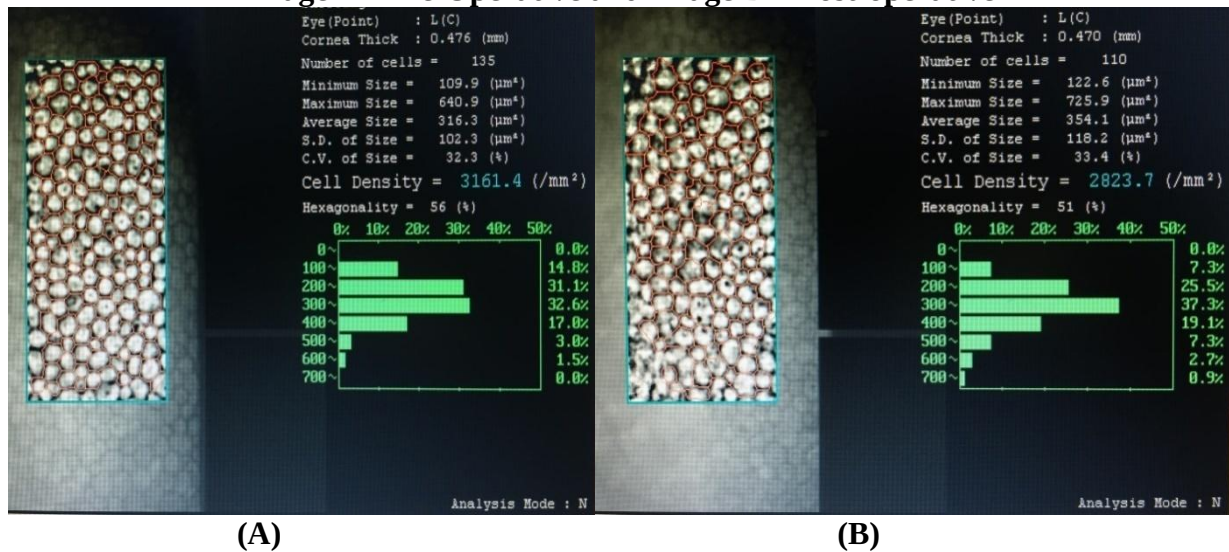
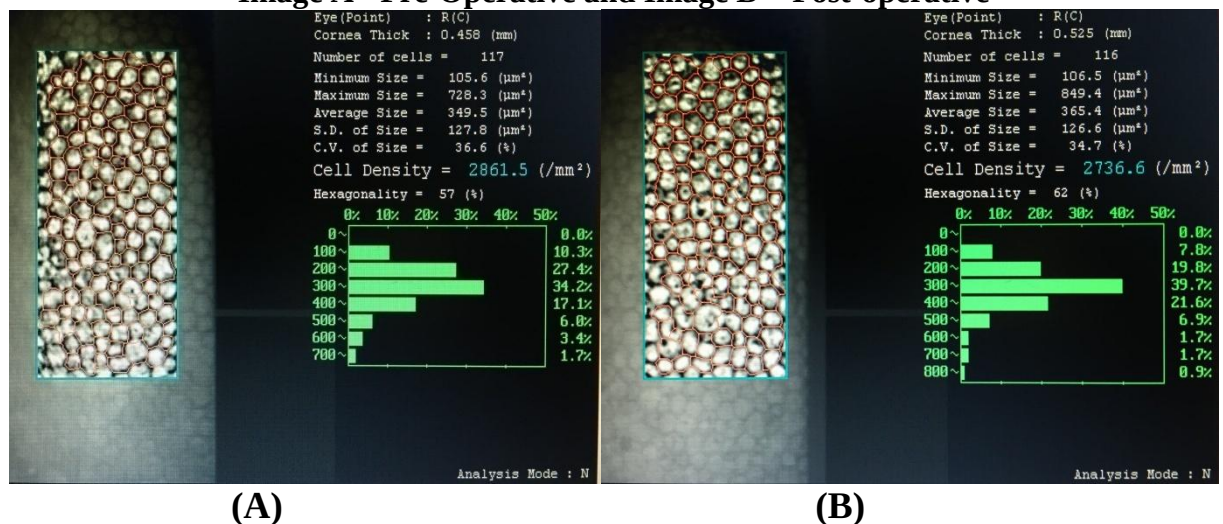


Figure 3
Specular microscopy in a Patient without Diabetes.
Image A= Pre-Operative and Image B = Post-operative



IV. DISCUSSION

This present study was conducted in upgraded department of ophthalmology, SMS Medical College, Jaipur with the aim to compare epithelial cell counts in diabetic and non diabetic group after phacoemulsification with intraocular lens implantation.

Both groups were comparable in age and sex wise. Pre-operative cell count, cell size, hexagonal cell counts, mean ECC, mean CV, UCVA and BCVA were also without significant difference in both the groups.

Post operatively it was observed in this study that there was a significantly greater corneal endothelial cell loss was observed in diabetic subjects compared with non-diabetic subjects 3 months after phacoemulsification with intraocular lens implantation.

Regarding mean Coefficient of Variance (CV), it was observed in this study that although within the group CV variations were with significant difference but the difference between the two groups was not significant statistically.

After the surgery the mean percentage of hexagonality dropped in both the groups but this decrease was significantly more in non-diabetic group.

Regarding visual acuity in this study, UCVA was found significantly increased in both the groups ($P < 0.001$) but the difference between the groups was not statistically significant. But BCVA was significantly increased in both the groups ($P < 0.001$) and it was significantly lesser in diabetic group than non diabetic group.

When both the group in Diabetic and Non-Diabetic were compare together as per cell size, it was found that post operatively cell size was without significant difference ($p > 0.05$).

Almost similar results were seen in the study conducted by Mikkel Hugod, MD et al ⁶ and Morikubo et al ⁷. Reshma Balan KT et al ⁸ also reported that diabetic patients undergoing Phacoemulsification had higher (19.06%) cell loss, when compared to non-diabetic patients who had 15.49% cell loss ($p = 0.022$) at the end of 6 months. One theory that can explain the fragility of the corneal endothelium in eyes of diabetic patients is the polyol osmotic theory Cogan DG Kinoshita JH Kador JH Nishimura PF et al ⁹⁻¹².

Although endothelial cell density is a widely used parameter for the status of the cornea after cataract surgery, it does not reflect the dynamics of the endothelial healing process that occurs in response to surgical trauma. The decrease in cell density reflects the surgical trauma itself, whereas the change in morphology is more closely associated with the process of repair. In this study, there was no statistical difference in the mean co-efficient of variance and hexagonality between the two groups in the pre-operative period.

Some recent studies have supported these early findings. Inoue et al ¹³ found a decrease in cell density and an increase in CV and concluded that the corneal endothelial cell structure was damaged. A recent study by Lee et al ¹⁴ concluded that patients with diabetes had increased CV and decreased endothelial cell density and percentage of hexagonal cells, as compared with that of the healthy controls.

In this study, there was no significant difference in the UCVA and BCVA between the two groups. This indicates that the higher cellular vulnerability probably only represents a minor elevation in the risk of corneal decompensation in patients with diabetes under good glycemic control.

V. CONCLUSION

It can be concluded from this study that there was a significantly greater corneal endothelial cell loss was observed in diabetic subjects compared with non-diabetic subjects 3 months after phacoemulsification with intraocular lens implantation. Mean Coefficient of Variance (CV) was observed in this study that although within the group CV variations were with significant difference but the difference between the two groups was not significant statistically. After the surgery the mean percentage of hexagonality dropped in both the groups but this decrease was significantly more in non-diabetic group.

Regarding visual acuity in this study, UCVA was found significantly increased in both the groups ($P < 0.001$) but the difference between the groups was not statistically significant. But BCVA was

significantly increased in both the groups ($P < 0.001$) and it was significantly lesser in diabetic group than non diabetic group

Despite good glycemic control and no corneal abnormalities before surgery, the endothelium in diabetic subjects is more vulnerable to surgical trauma and has a lower capability in the process of repair. These findings should be considered when planning cataract surgery in patients with diabetes. However, despite significant higher loss of endothelial cells and a significant slower process of cell repair in diabetic subjects, functional ocular status seemed unchanged as judged by CCT and visual acuity. Thus, a sufficient reserve capacity to maintain normal corneal functional status in well-controlled patients with diabetes exists during the period of follow-up.

CONFLICT

None declared till date.

REFERENCES

- [1] Mohan M. National Survey of Blindness-India. NPCB-WHO Report. New Delhi: Ministry of Health and Family Welfare, Government of India; 1989.
- [2] Mohan M. Collaborative Study on Blindness (1971-1974): A report. New Delhi, India: Indian Council of Medical Research; 1987. pp. 1-65
- [3] Andreas Pollreis Ursula Schmidt-Erfurth Diabetic Cataract—Pathogenesis, Epidemiology and Treatment Journal of Ophthalmology Volume 2010 (2010), Article ID 608751, 8 pages
- [4] Laing RA, Oak SS, Leibowitz HA: Specialized microscopy of the cornea. In: Leibowitz HM, Waring GO, eds. Corneal disorders. Philadelphia: W.B. Saunders; 1998:83-122
- [5] Yeh PC, Colby K: Corneal endothelial dystrophies. In: Foster CS, Azar DT, Dohlman CH, eds. Smolin and Thoft's the cornea. Philadelphia: Williams & Wilkins; 2005:849-874
- [6] Mikkel Hugod, MD, Allan Storr-Paulsen, MD, Jens Christian Norregaard, MD, PhD, DMSc, Jair Nicolini, MD, Allan Boye Larsen, MD, and Jesper Thulesen, MD, PhD, DMSc Corneal Endothelial Cell Changes Associated With Cataract Surgery in Patients With Type 2 Diabetes Mellitus Cornea 2011
- [7] Morikubo S, Takamura Y, Kubo E, et al. Corneal changes after small incision cataract surgery in patients with diabetes mellitus. Arch Ophthalmol. 2004;122:966-969
- [8] Reshma Balan KT, DO, MS, KV Raju, DO, MS Kerala Journal of Ophthalmology Vol. XXIV, No.1, Mar. 2012
- [9] Cogan DG Kinoshita JH Kador PF et al. NIH conference: aldose reductase and complications of diabetes. Ann Intern Med. 1984;101:82-91
- [10] Kinoshita JH Mechanisms initiating cataract formation: Proctor Lecture. Invest Ophthalmol. 1974;13:713-724
- [11] Kador PF The role of aldose reductase in the development of diabetic complication. Med Res Rev. 1988;8:325-352
- [12] Kinoshita JH Nishimura C The involvement of aldose reductase in diabetic complication. Diabetes Metab Rev. 1988;4:323-337
- [13] Inoue KKato S Inoue Y Amano S Oshika T The corneal endothelium and thickness in type II diabetes mellitus. Jpn J Ophthalmol. 2002;46:65-69
- [14] Lee JS, Oum BS, Choi HY, et al. Differences in corneal thickness and corneal endothelium related to duration in diabetes. Eye. 2006;20: 315-318