CORNEAL ENDOTHELIAL CELL DENSITY (ECD) AND CENTRAL CORNEAL THICKNESS (CCT) CHANGES IN TYPE-II DIABETICS AND NORMAL ADULTS AFTER MANUAL SMALL INCISION CATARACT SURGERY (MSICS)- A COMPARATIVE STUDY

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ABSTRACT

BACKGROUND
Corneal endothelium, the inner most layer of cornea, is a single layer of hexagonal cells, but other cell shapes are also present. This layer is responsible for maintaining the transparency of the cornea.
The aim of this study was to find out corneal endothelial cell density (ECD) and central corneal thickness (CCT) changes both pre- and post-operatively in Type II diabetics and normal adults who underwent Manual Small Incision Cataract Surgery (MSICS) with posterior chamber intraocular lens (PC IOL) implantation.

MATERIALS AND METHODS
The present study is a prospective, observational, comparative study which was done on patients who underwent manual small incision cataract surgery at Sarojini Devi Eye Hospital from October 2014 to August 2016 using a convenience non-random sampling method. The subjects were divided into two groups as per status of the diabetes: Diabetic group of 50 patients of Type II diabetics and Control group of 50 patients of normal adults. Subject's age ranged from 60 to 75 years. All patients underwent detailed eye examination including specular microscopy for ECD and CCT preoperatively. ECD and CCT were measured postoperatively on the 1st day, 1st week, 6th week and 12th week. Statistical analysis was done using independent sample student's t-test with SPSS version 17.0 software. Categorical data analysis was carried out using either chi-square test or Fisher's exact test as appropriate.

RESULTS
The mean preoperative ECD was 2621.9 ± 163.3 and 2371.1 ± 155.6 in control and diabetic groups respectively. The postoperative day one, 1st week, 6th week and 12th week's mean percentage of ECD was 5.5 ± 2.3, 6.4 ± 2.3, 7.7 ± 2.9 and 7.7 ± 2.5 respectively in control patients. It was 10.7 ± 2.7, 12.0 ± 2.4, 13.0 ± 2.4 and 13.6 ± 1.9 respectively in diabetic group. Post-operatively, the % ECD was significantly different between both the groups at each follow-up visit ($p < 0.0001$) for all. The mean preoperative CCT was 511.5 ± 21.4 and 517.7 ± 16.0 in control and diabetic groups respectively. The percent CCT was not significantly different between groups at each follow-up ($p > 0.005$) for all.

CONCLUSION
Compared to non-diabetic patients, diabetic patients showed more loss of corneal endothelial cells in the postoperative period. Central corneal thickness was more in diabetics when compared to non-diabetics, both pre- and post-operatively. Steps should be taken to minimise the insult to corneal endothelium during surgery.

KEY WORDS
ECD, CCT, Diabetics, MSICS, Specular Microscope.

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BACKGROUND

Corneal endothelium, the inner most is a single layer of hexagonal cells, but other cell shapes are also present. This layer is responsible for maintaining the transparency of the cornea. The endothelial cells have limited mitotic capacity, and any disturbance in the density of endothelial cells if it is below critical level (< 500 cells/ mm^2) might therefore have a profound effect on the transparency of cornea and vision.

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Changes in corneal epithelial and endothelial structure and function are commonly seen in Diabetes mellitus. Diabetes mellitus can cause changes in the cellular density and physiology of endothelial cells.[1]

All intraocular procedures that involve entry through anterior chamber produce some endothelial cell loss and cataract surgery is no exception.[2] The prevalence of cataract in adults above the age of 65 was roughly 13.5%, but in India more advanced stages of cataracts either with or without systemic problems are present, especially among rural population. Of the systemic problems, diabetes mellitus is more common with or without diabetic retinopathy. Because of large volumes of patients, lower operative expenditure, ease of technique and good post-operative results manual SICS with IOL implantation is the surgery of choice. There were very few reports from India on the effect of SICS on the corneal endothelium in diabetic patients. This study was undertaken to assess the postoperative endothelial cell loss and central corneal thickness in patients with type II diabetes undergoing manual SICS and to compare them with age-matched normal individuals.

Andhra Pradesh Eye Disease Study (APEDS 2000)[3] showed 18.7 million are blind, of which 9.5 million are cataract related causes with a prevalence of cataract at 69.8%. According to WHO,[4] Diabetes mellitus incidence in the world increases from 4.7% (108 million) in 1980 to 8.5% (422 million) in 2014 aged more than 18 years old and marked as World Health Day 2016 as 'action on diabetes.' In 2015 the diabetics in India are estimated to be 62 million and rising every year and reach about 100 million by 2030, the highest number by any country in the world. Diabetic retinopathy according to APEDS was 27%, of which majority are mild-to-moderate severity.[3]

Sarojini Devi Eye Hospital is a tertiary hospital with state of the art facilities for eye care services. Patients attending this institute are in large volumes with various eye diseases. Among surgical cases cataract occupies large proportion and patients coming not only from urban areas, but also from rural areas.

Diabetic corneas were significantly thicker than the normal corneas,[5] but there was no significant relation between central corneal thickness of diabetes and diabetes duration.[6] Diabetics frequently had abnormal corneal endothelium in contrast to normal persons,[7] but there were no significant differences in terms of function of the fluorescence permeability of the cornea[8,1,9] which means the corneal endothelium of diabetics has a structural disorder, but the function of the corneal tissues is not affected. It will take long time for diabetics to recover from damaged corneal tissue compared with normal persons.[1,10] As the corneal endothelium of diabetics has a structural disorder, a functional disorder of the diabetic corneal tissues can be caused by a stimulus like stress or trauma to the corneal tissue or from the lack of an adequate oxygen supply.[7] It is thought that diabetes reduces the activity of Na+-K+ ATPase of the corneal endothelium, and this causes the morphological changes and permeability changes in the corneas.[1,11]

MATERIALS AND METHODS

The present study is a prospective, observational, comparative study.

Inclusion Criteria

- Age group: 60 - 75 years.
- Patients operated by uneventful manual SICS.
- Preoperative cataract grading was done by Lens Opacity Classification System (LOCS III) and nuclear sclerosis (NS) grades II to III. All cortical cataract grades and all posterior sub-capsular opacity grades were included.
- All diabetics without diabetic retinopathy were included.

Exclusion Criteria

Patients who suffered or suffering with diseases that reduce or affect Endothelial Cell Density (ECD), eg. inflammations, glaucoma, trauma, congenital or hereditary eye diseases were excluded as they interfere with the present study. Age restrictions were due to depending on the patients that attended for MSICS. Patients more than 75 years were excluded due to their inability to participate in study. Complicated cataracts, hypermature cataracts with nuclear sclerosis more than grade III were also excluded from the study.

The sample size was calculated depending on the available patients during the said period, financial and other reasons. The sample size was adjusted and kept at 100, each 50 to reduce missing or lost data and to increase accuracy of study.

The study population consisted of 100 patients, of which 50 patients have diabetes mellitus type-II and 50 patients were controls (non-diabetics) who were age matched. All the patients underwent complete ophthalmic examination with slit lamp examination and gonioscopy. All patients were investigated for diabetic status like blood sugar and glycosylated haemoglobin (HbA1C). Endothelial cell density and central corneal thickness was measured by specular microscopy before installation of any mydriatic eye drops for fundus examination. Diabetics group patients and control group of non-diabetics underwent Manual Small Incision Cataract Surgery (MSICS) by same surgeon during the period from October 2014 to August 2016 at Sarojini Devi Eye Hospital, Hyderabad. The patients were evaluated by specular microscopy for endothelial cell density and central corneal thickness postoperatively on the 1st day, 1st week, 6th week and 12th week. 15 shots were taken in series and best image was automatically selected and displayed on the screen. The pre-installed software analysed the images automatically. The measurements were repeated thrice and the average value was taken into consideration.

Fifty eyes of 50 diabetic patients and 50 eyes of 50 non-diabetic patients underwent MSICS. All the eyes were dilated pre-operatively with tropicamide 0.8% and phenylephrine 5% eye drops. Surgeries were performed under peribulbar anaesthesia using of 5 mL of lignocaine 2% and bupivacaine 0.5% in ratio of 2: 1 with 150 units of hyaluronidase. Surgeries were conducted by a 6.5 mm frown scleral incision. Methyl cellulose 2% was used as viscoelastic. Nucleus was prolapsed into anterior chamber after performing capsulorhexis under trypan blue staining and delivered with wire vectis. Single piece polymethylmethacrylate intraocular lens was implanted in the bag after cortical aspiration. All surgeries were done by the same surgeon.

Data were analysed using SPSS version 17.0 software for windows. Descriptive statistical analysis was done. Results on continuous measurements were presented as mean and standard deviation. Statistical analysis was done using frequency distribution and significance tests, student T-test.

RESULTS

A total of 100 patients were included in this study, of which 50 were in control group and 50 in diabetic group. 24 males and 26 females were in control group, making it to 50 patients. 26 males and 24 females were in diabetic group, making it to 50 patients. The mean age of Diabetic group was 68.80 years and Non-diabetic group was 69.96 yrs. (Table 1).

		Diabetics (Mean ± S.D.)	Controls (Mean ± S.D.)
Mean Age		68.4 ± 4.1	69.3 ± 4.1
Gender	Male	24	26
	Female	26	24
LOCS III	NS II	23	23
	NS III	27	27

Table 1. Demographics and Lens Opacity Classification (LOCS III) of the Subjects

In the present study, Nuclear Sclerosis (NS) Grade II present in 23 cases (46%) and Nuclear Sclerosis (NS) Grade III (54%) present in 27 patients in each group were included. There was no statistically significant difference in lenticular opacity distribution between both diabetics and non-diabetics.

The mean pre-operative endothelial cell density was 2371.06 cells/mm² in diabetics and 2618.78 cells/mm² in controls. The mean pre-operative endothelial cell count in diabetic group was less than control group ($p < 0.001$), which was statistically significant (Table 2).

	Controls				Diabetics			
No.	ECD	Mean	Std. Dev	Std. Error of Mean	Mean	Std. Dev	Std. Error of Mean	P value
1	Preop	2621.98	163.294	23.093	2371.06	155.595	22.004	<0.001
2	Postop day 1	2494.00	176.070	24.900	2120.44	192.306	27.196	<0.001
3	Postop 1 wk.	2473.16	178.597	25.257	2088.18	185.132	26.182	<0.001
4	Postop 6 wks.	2438.88	177.001	25.032	2064.98	181.524	25.671	<0.001
5	Postop 12 wks.	2437.20	176.021	24.893	2049.34	167.464	23.683	<0.001

Table 2. Showing Endothelial Cell Density (ECD) Variations (Mean, Standard Deviation, Standard Error of Mean and P Value) at Each Visit

By comparing both the groups, mean endothelial density on the 1st postoperative day in diabetics was 2120.02 cell/mm² and 2495.56 cell/mm² in controls. The post-operative endothelial cell count in both groups were statistically significant ($p < 0.001$). By comparing endothelial loss in controls to diabetics post-operatively, the diabetic group had significantly higher endothelial loss ($p<0.001$). Mean endothelial cell density was 2049 cells/mm² and 2437cells/mm² in Diabetics and Controls at 12th week post-operatively (Figure 1).

The percentage change in Endothelial Cell Density (ECD) from baseline was significantly different between diabetic and non-diabetic patients at each follow-up visit ($p < 0.0001$ for all) (Table 3 and 4). The mean postoperative endothelial cell loss at 12th week were 322 cells/mm² in diabetic patients and 181 cells/mm² in control group.

	Controls				Diabetics		
No.	ECD	Mean	Std. Dev	Std. Error of Mean	Mean	Std. Dev	Std. Error of Mean
1	Preop	2621.98	163.294	23.093	2371.06	155.595	22.004
2	% day 1	5.5213	2.31902	0.33472	10.6868	2.66011	0.37620
3	% wk. 1	6.3580	2.34414	0.33835	12.0389	2.36190	0.33402
4	% wk. 6	7.6655	2.88338	0.41618	13.0063	2.37571	0.33598
5	% wk. 12	7.7294	2.51738	0.36335	13.6376	1.85926	0.26294

Table 3. Showing Endothelial Cell Density (ECD) Percentage Variations (Mean, Standard Deviation, and Standard Error of Mean) at Each Visit

	Controls				Diabetics			P-value
No.	ECD	Mean	Std. Dev	Std. Error of Mean	Mean	Std. Dev	Std. Error of Mean	
1	% day 1	5.5213	2.31902	0.33472	10.6868	2.66011	0.37620	<0.0001
2	% wk. 1	6.3580	2.34414	0.33835	12.0389	2.36190	0.33402	<0.0001
3	% wk. 6	7.6655	2.88338	0.41618	13.0063	2.37571	0.33598	<0.0001
4	% wk. 12	7.7294	2.51738	0.36335	13.6376	1.85926	0.26294	<0.0001

Table 4. Showing Endothelial Cell Density (ECD) Percentage Variations (Mean, Standard Deviation and Standard Error of Mean) from Baseline and its comparison between Diabetics and Controls

The percentage change in the central corneal thickness from baseline was not significantly different between diabetic and non-diabetic patients at each visit ($p > 0.05$ for all) (Table 5, 6 and Figure 2).

	Controls				Diabetics			
No.	CCT	Mean	Std. Dev	Std. Error of Mean	Mean	Std. Dev	Std. Error of Mean	P-value
1	Preop	511.46	21.434	3.03100	517.70	16.019	2.26500	0.019
2	Postop 1 wk.	534.46	24.837	0.37759	538.36	13.871	0.16426	0.291
3	Postop 6 wks.	534.96	24.639	0.38359	545.10	12.965	0.19688	0.008
4	Postop 12 wks.	524.02	30.267	0.19933	536.92	21.816	0.17794	0.005

Table 5. Showing Central Corneal Thickness (CCT) variations (Mean, Standard Deviation, Standard Error of Mean and P Value) at Each Visit

	Controls				Diabetics			P-value
No.	CCT	Mean	Std. Dev	Std. Error of Mean	Mean	Std. Dev	Std. Error of Mean	
1	% wk. 1	4.4643	2.64314	0.37759	3.8463	1.16150	0.16426	0.134
2	% wk. 6	4.5450	2.68510	0.38359	5.0371	1.39214	0.19688	0.254
3	% wk. 12	3.4733	1.35195	0.19933	4.0009	1.24556	0.17794	0.051

Table 6. Showing Central Corneal Thickness (CCT) Percentage variations (Mean, Standard Deviation and Standard Error of Mean) at each visit from Baseline and its comparison between Diabetics and Controls

DISCUSSION

Numerous studies were conducted to determine the effect of diabetes on corneal endothelial cell density and central corneal thickness after cataract surgery. Several studies indicated that diabetic patients have increased corneal vulnerability to intraocular surgical stress. Endothelial cell population is an important indicator of corneal health status and central corneal thickness, and hence effect of diabetes on corneal endothelium and CCT becomes an important parameter to study.

Endothelial alteration is considered an important parameter of surgical trauma. After any type of cataract surgery, with or without IOL implantation the corneal endothelial cell density is decreased than in healthy unoperated corneas. MSICS has become popular as a cost effective, suture less surgery with early visual rehabilitation for large scale cataract management in the developing world.[12]

In the present study, the mean preoperative endothelial cell count in diabetics and controls were 2371 cells/mm^2 and 2618 cells/mm^2 (p= < 0.001) respectively, in spite of good metabolic control. Studies conducted by Lee et al[13] (p<0.001), Ranganath et al[14] (p<0.001), Renu Dashmana[15] et al (p<0.001), Shenoy R et al[16] and Inoue et al[17] reported less number of endothelial cells in diabetics as compared to non-diabetics. A study conducted in southern India with a large study sample also showed that the mean endothelial cell density was of significantly low across all ages in patients with type II diabetics compared to non-diabetics. The results of the present study are similar to those studies mentioned above.

In the present study mean endothelial cell count post-operatively at 12th week in diabetic group was 2049.34 cells/mm^2 and in control group was 2437.20 cells/mm^2. The day 1, week 1, week 6 and week 12 mean percentage of ECD was 5.5 ± 2.3, 6.4 ± 2.3, 7.7 ± 2.9 and 7.7 ± 2.5 respectively in control patients and was 10.7 ± 2.7, 12.0 ± 2.4, 13.0 ± 2.4 and 13.6 ± 1.9 respectively in diabetic group. There was a progressive decrease in endothelial count in both groups post-operatively till 12 weeks. This endothelial loss was more in diabetic group as compared to control group and was statistically significant (p < 0.001). Studies conducted by Lee et al,[13] Hugod et al[18] (p= 0.004) and Renu Dashmana[12] et al (p<0.001) showed decrease in endothelial cell density post-operatively, which is consistent with the present study. Study done by Morikubo[19] et al and Mathew et al[20] showed that there was less functional reserve. Despite the decrease in endothelial count in diabetic group, none of them developed corneal decompensation.

In the present study mean central corneal thickness in diabetic group (517.34 µ) was more than control group (511.46 µ) preoperatively, which was significant (p= 0.019). Study done by Renu Dasmana[15] also showed the CCT was higher in diabetes preoperatively (p= 0.005). In the present study, CCT increased post-operatively in both the groups (p<0.001) at 12 weeks. In diabetic group (536.10 µ), the cornea was much thicker than in control group (520.80 µ). The percent CCT was not significantly different between groups at each follow-up (p > 0.005 for all). Cornea in diabetic group takes longer time to recover compared to non-diabetics. Renu Dasmana[15] et al, Morikubo[19] et al and Mathew[20] et al in their study of changes in corneal endothelium and central corneal thickness in diabetic patients, there was increase in CCT post-operatively in diabetic group compared to control group which supports the present study. It is thought that in diabetics, aldose reductase which acts as osmotic agent leads to swelling of endothelial cells by intracellular accumulation of polyol. The activity of Na+-K+ ATPase is reduced in diabetic corneal endothelium and this causes morphological and functional changes of diabetic corneas. The limitations of the present study were the small sample size and the follow-up period was also of short duration.

CONCLUSION

Preoperatively, diabetic patients have lesser endothelial cell density (ECD= 2371.06 cells/mm^2 ± 155.59) when compared to controls (ECD= 2618.78 cells/mm^2 ± 174.81). Preoperatively, central corneal thickness (CCT) in diabetics is 517.74 µm ± 15.89 µ when compared to controls, CCT= 511.76 µm± 2.43 µ respectively.

Postoperatively, diabetic patients showed more endothelial cell loss (322 cells/mm^2), 13.64% when compared to controls (118 cells/mm^2) 7.73%. The central corneal thickness is increased (536.10 µm ± 14.87) in diabetics when compared to controls (524.02 µm ± 36.37), but the percentage of CCT was not significantly different between groups at each follow-up (p > 0.005 for all).

The endothelial cell loss in diabetics neither led to corneal decompensation nor produced visual disability. Compared to control patients, diabetic patients showed more loss of corneal endothelial cells with operative stress and delay in recovery of corneal oedema after manual small incision cataract surgery. The endothelial cell loss was more in diabetics with small incision cataract surgery. In patients with critically low corneal endothelial density, this type of loss can produce corneal decompensation and visual disability. Central corneal thickness was more in diabetics when compared to non-diabetics both pre- and post-operatively. Post-operatively, central corneal thickness increased when compared to non-diabetics, but percentage change was not significant.

REFERENCES

[1] Tuft SJ, Coster DJ. The Corneal endothelium. Eye (Lond) 1990;4(Pt 3):389-424.

[2] McCarrey BE, Edelhauser HF, Lynn MJ. Review of corneal endothelial specular microscopy for FDA clinical trials of refractive procedures, surgical devices and new intraocular drugs and solutions. Cornea 2008;27(1):1-16.

[3] Dandona R, Dandona L. Review of findings of Andhra Pradesh eye disease study: policy implications for eye-care services. Current J Ophthalmology 2001;49(4):215-34.

[4] WHO. Global data on visual impairments 2010.

[5] Su DH, Wong TY, Wong WL, et al. Diabetes, hyperglycemia and central corneal thickness: The Singapore Malay Eye Study. Ophthalmology 2008;115(6):964-8.e1.

[6] Measurements of the thickness of the cornea. Arch Ophthal (Paris) 1971;31:529-88.

[7] Schultz RO, Matsuda M, Yee RW, et al. Corneal endothelial changes in type I and type II diabetes mellitus. Am J Ophthalmol 1984;98(4):401-10.

[8] Watsky MA, McDermott ML, Edelhauser HF. In vitro corneal endothelial permeability in rabbit and human: the effects of age, cataract surgery and diabetes. Exp Eye Res 1989;49(5):751-67.

[9] Keoleian GM, Pach JM, Hodge DO, et al. Structural and functional studies of the corneal endothelium in diabetes mellitus. Am J Ophthalmol 1992;113(1):64-70.

[10] Ziadi M, Moiroux P, d'Athis P, et al. Assessment of induced corneal hypoxia in diabetic patients. Cornea 2002;21(5):453-7.

[11] Sturrock GD, Sherrard ES, Rice NS. Specular microscopy of the corneal endothelium. BJO 1978;62(12):809-14.

[12] Busted N, Olsen T, Schmitz O. Clinical observations on corneal thickness and the corneal endothelium in diabetes mellitus. Br J Ophthalmol 1981;65(10):687-90.

[13] Lee JS, Oum BS, Choi HY, et al. Differences in corneal thickness and corneal endothelium in related to duration of diabetes. Eye (Lond) 2006;20(3):315-8.

[14] Parekh R, Ranganath KN, Suresh KP, et al. Corneal endothelium count and thickness in diabetes mellitus. Int J Diab Dev Ctries 2006;26(1):24-6.

[15] Dasmana R, Singh IP, Nagpal RC. Corneal changes in diabetic patients after manual small incision cataract surgery. J Clin Diagn Res 2014;8(4):VC03-VC06.

[16] Shenoy R, Khandekar R, Bialasiewicz A, et al. Corneal endothelium in patients with diabetes mellitus: a historical cohort study. Eur J Ophthalmol 2009;19(3):369-75.

[17] Inoue K, Kato S, Inoue Y, et al. The corneal endothelium and thickness in type II diabetes mellitus. Jpn J Ophthalmol 2002;46(1):65-9.

[18] Hugod M, Storr-Paulsen A, Norregaard JC, et al. Corneal endothelial cell changes associated with cataract surgery in patients with type 2 diabetes mellitus. Cornea 2011;30(7):749-53.

[19] Morikubo S, Takamura Y, Kubo E, et al. Corneal changes after small-incision cataract surgery in patients with diabetes mellitus. Arch Ophthalmol 2004;122(7):966-9.

[20] Mathew PT, David S, Thomas N. Endothelial cell loss and central corneal thickness in diabetic patients with and without diabetes after manual small incision cataract surgery. Cornea 2011;30(4):424-8.