DOI: 10.7860/JCDR/2023/53735.18197

Original Article

Ophthalmology Section

Central Corneal Thickness and Endothelial Cell Changes after Phacoemulsification in Patients with Diabetes Mellitus: A Prospective Study

HANS RAJ SHARMA[1], ANUREET KAUR[2], ASHOK K SHARMA[3], ASMA JABEEN[4], ROHINI CHOUDHARY[5]

ABSTRACT

Introduction: Diabetes Mellitus (DM) has emerged as a significant cause of ocular morbidity. The toxic effects of hyperglycaemia spare no cell in the body and cornea, has also revealed certain changes in diabetic patients. Higher phacoemulsification time and power effect corneal endothelial cells. This can inflict an additional stress on the altered diabetic corneal endothelium.

Aim: To compare the Central Corneal Thickness (CCT) thickness and endothelial Cell Density (CD) and morphology in Type 2 Diabetes Mellitus (T2DM) patients undergoing phacoemulsification with age-matched non diabetic controls undergoing phacoemulsification.

Materials and Methods: A prospective, hospital-based, interventional study was conducted in the Department of Ophthalmology, Government Medical College, Jammu, Jammu and Kashmir, India. The duration of the study was nine months, from April 2021 to December 2021. The study included 50 patients with T2DM and 50 non diabetic controls. All patients underwent phacoemulsification performed by a single surgeon. The CCT and endothelial cell parameters were measured preoperatively and postoperatively at one week, six weeks and three months using Topcon specular microscope. Postoperative changes in the corneal endothelial cells were compared between the two groups for a period of three months. Statistical analysis was done by using the Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corp. Released 2017. Armonk, NY, USA). Categorical variables were analysed using Chi-square test and the groups were compared using Student's t-test.

Results: The mean age of the study participants was 63.22±7.52 years in diabetic group and 64.52±7.29 years in non diabetic group. Diabetic patients showed significantly greater corneal thickness than non diabetic controls (p=0.034). This pattern was observed till the last follow-up at three months. The endothelial cell parameters were comparable between diabetic and non diabetic patients. There was a fall in endothelial cell count in all patients postoperatively, but it was significantly higher in the diabetic patients at three months (p=0.048). Postoperatively, Coefficient of Variation (CV) was significantly higher in diabetic patients (p=0.001) accompanied by a decreased hexagonality (p=0.039) at the end of three months.

Conclusion: A diabetic cornea is different than a non diabetic cornea at the cellular level. Diabetics show accelerated corneal endothelial cell loss and greater variation in cell morphology in response to surgical stress. Diabetes mellitus is a risk factor for endothelial cell loss in patients undergoing cataract surgery.

Keywords: Cataract surgery, Cornea, Hyperglycaemia, Ocular morbidity

INTRODUCTION

The corneal endothelial cells decrease in density with increasing age and this is exaggerated by trauma and intraocular surgery. Phacoemulsification causes endothelial cell loss due to intraoperative mechanical trauma. Higher grades of nuclear sclerosis require more phaco power and increase the Effective Phaco Time (EPT) which is a risk factor for augmented endothelial cell damage [1]. This endothelial cell loss and dysfunction leads to water imbibition by cornea increasing the corneal thickness. Inspite of the advances in phacoemulsification techniques and the use of viscoelastic agents, central corneal endothelial cell loss after phacoemulsification occurs around 4% to 15% [2]. The diabetic cornea is particularly susceptible to trauma and has dysfunctional repair mechanisms. Many explanations have been hypothesised to explain this dysfunction. Diabetics frequently develop hyperglycaemia in the aqueous, which causes inhibition of the Sodium-Potassium Adenosine Triphosphatase (Na^+/K^+-ATPase) of the corneal endothelium compromising corneal deturgescence [3]. Diabetics frequently have poor pupillary dilatation, which increases surgical difficulty. Compromised endothelial pump function, the extent of intraocular inflammation and increased surgical time, may lead to increased incidence of corneal oedema in diabetic patients [4]. Other studies have revealed altered endothelial cell morphology in diabetic corneas [5,6].

A diabetic cornea loses about five times more endothelial cells per one second EPT than non diabetics and hence, is more prone to develop complications of corneal decompensation and pseudophakic bullous keratopathy [7]. Phacoemulsification in a patient of T2DM can impose a great risk of long term endothelial cell dysfunction. Corneal endothelial evaluation should be performed in all diabetics along with routine fundus examination. The aim of the present study was, to compare the CCT and endothelial CD and morphology in T2DM patients, who were undergoing phacoemulsification.

MATERIALS AND METHODS

This prospective, hospital-based, interventional study was conducted in the Department of Ophthalmology, Government Medical College, Jammu, Jammu and Kashmir, India. The duration of the study was nine months, from April 2021 to December 2021. Approval was taken from the Institutional Ethics Committee (No: IEC/GMC/Cat C/2021/513).

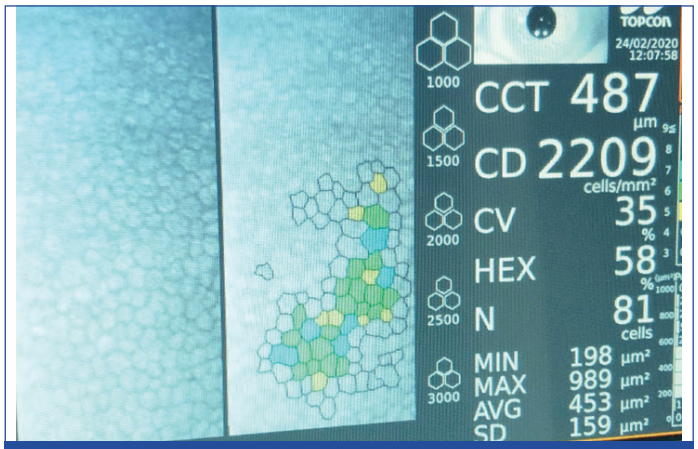
Inclusion criteria: Patients of either gender ≥40 years of age with senile cataract (nuclear sclerosis ≤grade III) and scheduled to undergo phacoemulsification with posterior chamber Intraocular Lens (IOL) implantation, were included in the study.

Exclusion criteria: Patients with high myopia >6 diopters (D), corneal opacities and dystrophies, pseudoexfoliation, uveitis, glaucoma, previous history of intraocular surgery or trauma, complicated cataract surgery and endothelial cell count <1500 cell/mm^2. Additionally,

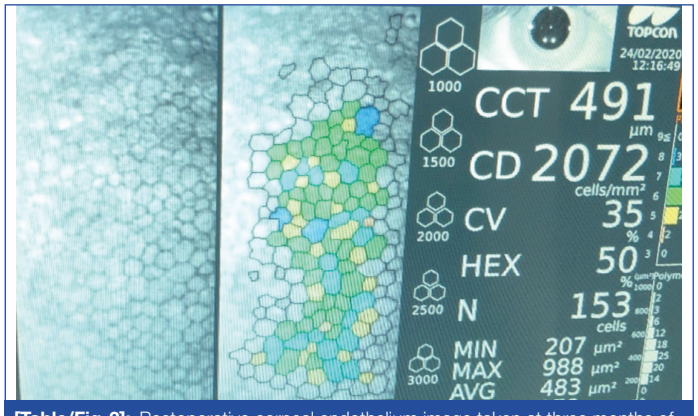
patients with DM and deranged glycated haemoglobin (HbA1c) levels were excluded from the study.

Study Procedure

The study included two groups: Group 1 comprised of 50 diabetic patients, who were non insulin dependent type 2 diabetics with good control of blood sugar and Group 2 comprised of 50 non diabetic patients. The participants were selected by convenient sampling after taking written and informed consent. Both groups underwent phacoemulsification using same technique. The details and motive of the study were explained to each patient and after obtaining an informed written consent, they were enrolled in the study. After thorough history taking, general physical examination and local examination were performed including visual acuity with Snellen's vision drum, slit lamp examination, fundus examination and tonometry. Systemic investigations conducted were routine urine examination, complete blood count, fasting and postprandial blood sugar, HbA1c levels, chest X-ray, viral markers such as Human Immunodeficiency Virus (I and II) (HIV), Hepatitis B Virus (HBV), and Hepatitis C Virus (HCV). The CCT and endothelial cell parameters- CD, CV of cell size and Hexagonality of Cells (HC) were measured using Topcon specular microscope by the same observer [Table/Fig-1]. All the patients underwent phacoemulsification using 'stop and chop' technique by a single surgeon. Intraoperative mydriasis, phacoemulsification time and power (EPT) used were noted. Postoperatively CCT, endothelial CD, CV and percentage of hexagonal cells were assessed at week one, week six and three months [Table/Fig-2].



[Table/Fig-1]: Preoperative corneal endothelium image taken by Topcon clinical specular microscope of a 61-year-old diabetic female.



[Table/Fig-2]: Postoperative corneal endothelium image taken at three months of the same patient as shown in [Table/Fig-1].

STATISTICAL ANALYSIS

Statistical analysis was done by using the Statistical Package for Social Sciences (SPSS) version 25.0 (IBM Corp. Released 2017. Armonk, NY, USA). Categorical variables were represented as number and percentage and analysed using Chi-square test. The continuous variables of the two groups were represented as mean±SD and were compared using Students' t-test. Preoperative versus postoperative modifications within the groups were verified using two-way repeated measures Analysis of Variance (ANOVA). All statistical tests were carried out at 5% level of significance and p<0.05 was considered statistically significant.

RESULTS

In the present study, corneal endothelial cell parameters in 50 eyes of diabetic patients were compared with 50 eyes of non diabetic patients undergoing phacoemulsification. In diabetic group, there were 26 (52%) males and 24 (48%) females whereas, non diabetic group consisted of 34 (68%) males and 16 (32%) females (p=0.10). The mean age of the patients was 63.22±7.52 years in diabetic group and 64.52±7.29 years in non diabetic group (p=0.40). The difference in age and gender distribution between both the groups was statistically not significant. The mean pupil size in diabetic group was 6.86±0.73 mm and in non diabetic group was 7.00±0.58 mm. The difference in intraoperative pupil size between the two groups was statistically not significant. The mean EPT in patients of diabetic group was 9.96±4.15 seconds and in non diabetic group was 9.89±6.37 seconds. No statistically significant difference was observed in the EPT between the two groups [Table/Fig-3].

Variables		Group 1	Group 2	p-value
Age (in years)		63.22±7.52	64.52±7.29	0.40#
Gender	Male	26	34	0.10*
	Female	24	16	
Pupil size (mm)		6.86±0.73	7.00±0.58	0.29#
EPT (seconds)		9.96±4.15	9.89±6.37	0.33#

[Table/Fig-3]: Comparison of demographic characteristics and operative parameters.
*Chi-square test; #Student's t-test

Preoperatively, the mean CCT in diabetic group was 517.52±18.796 µm and in non diabetic group was 506.60±30.621 µm. The thickness of cornea was more in group 1 as compared to group 2 and the difference was statistically significant (p=0.034). Postoperatively, there was a significant increase in CCT in both the groups (p=0.001). The CCT in group 1 was significantly higher than in group 2 at all follow-up visits (p=0.043 at one week, p=0.040 at six weeks and p=0.025 at three months). However, the increase in intragroup CCT after three months from baseline was similar between the two groups (p=0.818) [Table/Fig-4].

Central Corneal Thickness (CCT)	Group 1	Group 2	p-value#
Pre-op	517.52±18.796	506.60±30.621	0.034
Post-op one week	546.06±21.254	533.34±38.393	0.043
Post-op six weeks	531.60±22.083	519.78±33.585	0.040
Post-op three months	522.98±20.403	510.94±31.463	0.025
Difference between pre-op and three months post-op	4.08±4.08 (0.78%)	4.34±6.83 (0.85%)	0.818
p-value of difference between pre-op and three months post-op	0.001*	0.001*	

[Table/Fig-4]: Comparison of preoperative and postoperative Central Corneal Thickness (CCT) between the two groups (µm).
#Student's t-test, *One-way ANOVA. The percentages were calculated as: Calculated by taking the difference as numerator and pre-op value as denominator

The mean preoperative CD in group 1 was 2633.06±207.491 cells/mm^2 and in group 2 was 2646.40±296.885 cells/mm^2. The difference in baseline CD in both the groups was not statistically significant (p=0.795). Postoperatively, the decrease in CD in both the groups was statistically significant (p=0.001). On comparing intergroup change, the CD in group 1 was significantly less than in group 2 at all levels of follow-up (p=0.020 at one week, p=0.034 at six weeks and p=0.028 at three months). At the end of three months, the endothelial cell loss in group 1 was significantly higher than in group 2 (p=0.048) [Table/Fig-5].

Cell Density (CD)	Group 1	Group 2	p-value#
Pre-op	2633.06±207.491	2646.40±296.885	0.795
Post-op one week	2102.02±204.067	2245.28±376.357	0.020
Post-op six weeks	1992.06±228.326	2136.46±416.571	0.034
Post-op three months	1942.74±211.804	2087.98±410.009	0.028
Difference between pre-op and three months post-op	690.320±163.282 (26.21%)	558.420±436.462 (21.10%)	0.048
p-value of difference between pre-op and three months post-op	0.001*	0.001*	

[Table/Fig-5]: Comparison of preoperative and postoperative endothelial Cell Density (CD) between the two groups (cells/mm²).
ECD: Endothelial cell density; #Student's t-test, *one-way ANOVA. The percentages were calculated as- Calculated by taking the difference as numerator and pre-op value as denominator

Preoperatively, the mean CV in group 1 was 31.82±4.163 and in group 2 was 30.98±2.352. The CV in group 1 was more than in group 2 but the difference was not statistically significant (p=0.217). There was a significant increase in CV in both the groups postoperatively (p=0.001). The mean CV of group 1 was higher than that of group 2 but the difference was not statistically significant at one week and six weeks follow-up (p=0.839, 0.374, respectively). However, at three months, the mean CV in group 1 was significantly higher than group 2 (p=0.001) [Table/Fig-6].

Coefficient of Variation (CV)	Group 1	Group 2	p-value#
Preoperative	31.82±4.163	30.98±2.352	0.217
Post-op one week	35.36±3.890	35.52±3.965	0.839
Post-op six weeks	35.00±3.393	34.42±3.091	0.374
Post-op three months	38.54±4.652	33.96±2.878	0.001
Difference between pre-op and three months post-op	6.720±3.104 (21.19%)	2.980±3.408 (9.61%)	0.001
p-value of difference between pre-op and three months post-op	0.001*	0.001*	

[Table/Fig-6]: Comparison of preoperative and postoperative Coefficient of Variation (CV) between the two groups (cells/mm²).
#Student's t-test, *one-way ANOVA. The percentages were calculated by taking the difference as numerator and pre-op value as denominator; Pre-op: Preoperative; Post-op: Postoperative

The mean preoperative percentage of hexagonal cells in group 1 was 53.24±6.748 while in group 2 was 54.04±5.757. The difference in hexagonality between the two groups was not statistically significant (p=0.525). There was a decrease in percentage of hexagonal cells in both the groups postoperatively (p=0.001). At one week, the mean hexagonality in group 1 was less than in group 2 but the difference was not statistically significant (p=0.276). At six weeks and three months, the difference between the two groups was statistically significant (p=0.044, 0.039, respectively). Three months postoperatively, the mean loss of hexagonal cells in group 1 was more than in group 2 but the difference was not significant (p=0.137) [Table/Fig-7].

Hexagonal Cells (HC)	Group 1	Group 2	p-value#
Pre-operative	53.24±6.748	54.04±5.757	0.525
Post-op one week	49.94±5.676	51.18±5.638	0.276
Post-op six weeks	48.36±5.122	50.50±5.342	0.044
Post-op three months	47.44±5.541	49.76±5.535	0.039
Difference between pre-op and three months post-op	5.800±5.241 (10.9%)	4.280±4.891 (7.92%)	0.137
p-value of difference between pre-op and three months post-op	0.001*	0.001*	

[Table/Fig-7]: Comparison of preoperative and postoperative percentage of Hexagonal Cells (HC) between the two groups.
#Student's t-test, *one-way ANOVA. The percentages were calculated as- Calculated by taking the difference as numerator and pre-op value as denominator

DISCUSSION

Diabetes mellitus is a significant cause of ocular morbidity [8]. Around 70% diabetics have impaired corneal function described as diabetic keratopathy [9]. Earlier studies have shown structural differences in the endothelial cells of the diabetic cornea [5,10]. Manipulations in the cornea and anterior chamber as occurs in phacoemulsification can be detrimental for the diabetic endothelium. The patients in the present study were age and sex matched. No statistically significant difference was observed in the mean pupillary size between the diabetic and non diabetic groups (p=0.291). The intergroup comparison of mean EPT was not statistically significant (p=0.948). Similar results were revealed in a study by Ganesan N et al., [4]. In the present study, the baseline CCT of diabetic group was 517.52±18.796 µm and of non diabetic group was 506.60±30.621 µm (p=0.034). Similarly, studies conducted by Lee JS et al., and Kudva AA et al., also reported increased CCT of the diabetic corneas [11,12]. It is speculated that in diabetics, aldose reductase causes accumulation of sorbitol in corneal layers which causes swelling of the cornea by osmosis [13]. Postoperatively, the difference in CCT was more in diabetics as compared to non diabetics on all follow-up visits (p=0.043 at one week, p=0.040 at six weeks). At three month, the mean CCT in diabetic group was 522.98±20.403 µm and in non diabetic group was 510.94±31.463 µm (p=0.025). A study conducted by Elbassiouny O et al., concluded significant difference in CCT in diabetics postoperatively at one month due to delayed endothelial recovery [14].

In present study, preoperatively, the mean ECD in diabetic group was 2633.06±207.491 cells/mm² and in non diabetic group was 2646.40±296.885 cells/mm². No significant difference was found in the preoperative Endothelial Cell Density (ECD) between the two groups (p=0.795). The result of the present study was in agreement with studies conducted by Schultz RO et al., and Inoue K et al., [15,16]. The endothelial cell count showed progressive decrease in the postoperative period. However, this endothelial cell loss was more pronounced in the diabetic group as compared to the non diabetic group at one week, six weeks and three month follow-up (p=0.020, p=0.034 and p=0.028, respectively). In favour, Khalid M et al., observed that, two months after phacoemulsification, the mean ECD was less in the diabetics, group than in the non diabetic group [17]. Hugod M et al., showed a mean endothelial cell loss of 6.2% in diabetics while only 1.4% in the non diabetic controls three months after surgery (p=0.04) [18]. The diabetic cornea is more vulnerable to surgical stress as compared to the non diabetic cornea.

Preoperatively, the mean CV in diabetic group was 31.82±4.163 and in non diabetic group was 30.98±2.352. The baseline CV values were comparable between the two groups (p=0.217). The CV values increased in both the groups postoperatively, but the intergroup difference was not statistically significant till six weeks follow-up (p=0.374). Likewise, Khan A et al., reported no significant difference in baseline CV values between the two groups (p=0.86) [19]. At three months, the mean CV in diabetic group was 38.54±4.652 whereas in non diabetic group was 33.96±2.878. The increase in CV was significantly more in diabetics than non diabetics only at three month follow-up (p=0.001). Al-Sharkawy HT showed no significant difference in CV values in both the groups preoperatively, but at three months postoperatively, the increase in CV was significantly more in diabetic patients than in controls (p=0.01) [20].

In the present study, preoperatively, the percentage of hexagonal cells in diabetic group was 53.24±6.748 and in non diabetic group was 54.04±5.757. No difference was revealed in mean hexagonality between the two groups (p=0.525). Postoperatively, the change in hexagonality was similar in both the groups at one week (p=0.276) but the hexagonality was significantly more in non diabetics as compared to diabetics at six weeks (p=0.044) and three months (p=0.039). Ganesan N et al., reported that at three month, the percentage of hexagonal cells in diabetic group was significantly less than the non diabetic group (p=0.01) [4]. Diabetics have decreased percentage of hexagonality and significant increase in coefficient of

variation in cell size which reveals that, the morphological changes in cornea of diabetics are associated with low functional reserve.

Limitation(s)

The study was limited by small sample size. It did not include the duration of diabetes and the status of retinopathy in the diabetic population. Considering these factors in a study, will give a more accurate reflection of the impact of diabetes mellitus, on corneal endothelium and its behaviour in the event of surgical stress.

CONCLUSION(S)

The present study revealed increased baseline thickness of the diabetic cornea as compared to non diabetic corneas. After phacoemulsification, diabetic corneas showed more endothelial cell loss along with structural alterations in the cells. CCT of diabetic corneas was more than non diabetics which returned to preoperative levels after three months. It was observed that, the diabetic cornea manifests more changes than the non diabetic cornea after phacoemulsification and corneal endothelium should be assessed in patients undergoing cataract surgery.

Acknowledgement

The authors would like to thank the contributions of Dr. Palak Gupta and Dr. Arjumand Nazir in the conduct of the present study.

REFERENCES

[1] Pirazzoli G, D'Eliseo D, Ziosi M, Acciarri R. Effects of phacoemulsification time on the corneal endothelium using phacofracture and phaco chop techniques. J Cataract Refract Surg. 1996;22(7):967-69.
[2] Ho JW, Afshari NA. Advances in cataract surgery: Preserving the corneal endothelium. Curr Opin Ophthalmol. 2015;26(1):22-27.
[3] Whikehart DR, Montgomery B, Angelos P, Sorna D. Alteration of ATPase activity and duplex DNA in corneal cells grown in high glucose media. Cornea. 1993;12(4):295-98.
[4] Ganesan N, Srinivasam R, Babu KR, Vallinayagam M. Risk factors for endothelial cell damage in diabetics after phacoemulsification. Oman J Ophthalmol. 2019;12(2):94-98.
[5] Shenoy R, Khandekar R, Bialasiewicz A, Al Muniri A. Corneal endothelium in patients with diabetes mellitus: A historical cohort study. Eur J Ophthalmol. 2009;19(3):369-75.
[6] El-Agamy A, Alsubaie S. Corneal endothelium and central corneal thickness changes in type 2 diabetes mellitus. Clin Ophthalmol. 2017;11:481-86.
[7] Ghita AC, Ghita AM, Alexandrescu C. The effects of cataract surgery on endothelial cells in diabetic patients. Proc Rom Acad. 2015;1:100-04.
[8] Sayin N, Kara N, Pekel G. Ocular complications of diabetes mellitus. World J Diabetes. 2015;6(1):92-108.
[9] Lutty GA. Effects of diabetes on the eye. Invest Ophthalmol Vis Sci 2013;54(14):ORSF81-87.
[10] Sudhir RR, Raman R, Sharma T. Changes in the corneal endothelial cell density and morphology in patients with type 2 diabetes mellitus: A population-based study, Sankara Nethralaya Diabetic Retinopathy and Molecular Genetics Study (SN-DREAMS, Report 23). Cornea. 2012;31(10):1119-22.
[11] Lee JS, Lee JE, Choi HY, Oum BS. Corneal endothelial cell change after phacoemulsification relative to the severity of diabetic retinopathy. J Cataract Refract Surg. 2005;31(4):742-49.
[12] Kudva AA, Lasrado AS, Hegde S, Kadri R, Devika P, Shetty A. Corneal endothelial cell changes in diabetics versus age group matched non diabetics after manual small incision cataract surgery. Indian J Ophthalmol. 2020;68(1):72-76.
[13] Zhao H, He Y, Ren YR, Ghen BH. Corneal alteration and pathogenesis in diabetes mellitus. Int J Ophthalmol. 2019;12(12):1939-50.
[14] Elbassiouny O, Khalil A, Elnahrawy O, Rashid A. Corneal endothelial changes in correlation with corneal thickness after phacoemulsification among diabetic patients. Adv Ophthalmol Vis Syst. 2017;7(1):00208.
[15] Schultz RO, Matsuda M, Yee RW, Edelhauser HF, Schultz KJ. Corneal endothelial changes in type I and type II diabetes mellitus. Am J Ophthalmol. 1984;98(4):401-10.
[16] Inoue K, Kato S, Inoue Y, Amano S, Oshika T. The corneal endothelium and thickness in type II diabetes mellitus. Jpn J Ophthalmol. 2002;46(1):65-69.
[17] Khalid M, Hanif MK, Islam QU, Mehboob MA. Change in corneal endothelial cell density after phacoemulsification in patients with type II diabetes mellitus. Pak J Med Sci. 2019;35(5):1366-69.
[18] Hugod M, Storr-Paulsen A, Norregaard JC, Nicolini J, Larsen AB, Thulesen J. Corneal endothelial cell changes associated with cataract surgery in patients with type 2 diabetes mellitus. Cornea. 2011;30(7):749-53.
[19] Khan A, Kose S, Jharwal MK, Meena A, Sharma A. Comparison of corneal endothelial cell counts in patients with controlled diabetes mellitus (Type 2) and non diabetics after phacoemulsification and intraocular lens implantation. Int Multispecialty J Health. 2016;2:14-22.
[20] Al-Sharkawy HT. Corneal endothelial changes in type 2 diabetes mellitus before and after cataract surgery. J Egypt Ophthalmol Soc. 2015;108(2):79-85.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Ophthalmology, Government Medical College, Jammu, Jammu and Kashmir, India.
2. Resident, Department of Ophthalmology, Government Medical College, Jammu, Jammu and Kashmir, India.
3. Professor, Department of Ophthalmology, Government Medical College, Jammu, Jammu and Kashmir, India.
4. Resident, Department of Ophthalmology, Government Medical College, Jammu, Jammu and Kashmir, India.
5. Resident, Department of Ophthalmology, Government Medical College, Jammu, Jammu and Kashmir, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Anureet Kaur,
Near Sampark National Highway, Kunjwani,
Jammu-180010, Jammu and Kashmir, India.
E-mail: anureet7691@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 10, 2022
- Manual Googling: Nov 09, 2022
- iThenticate Software: Dec 15, 2022 (15%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Jan 06, 2022**
Date of Peer Review: **Apr 07, 2022**
Date of Acceptance: **Dec 31, 2022**
Date of Publishing: **Jul 01, 2023**