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Evaluation of Corneal Endothelial Cell Count and Morphology in Patients with Diabetes Mellitus

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Abstract

Background: The metabolic condition known as diabetes mellitus is characterized by persistently high blood sugar levels and alterations in fat and protein metabolism as well as problems in insulin secretion or action, or both.

Material and Methods: Patients with diabetes mellitus referred to the KIMS Hospital, Department of General Medicine are referred to the Department of Ophthalmology for a comprehensive examination of the cornea's endothelial cell count and appearance. Descriptive and prospective cross-sectional research.

Results: There is a statistically significant reduction in endothelial cell density between the diabetes population and the non-diabetic control group, with the former having a mean of 2448.145 +/- 245.77 cells per sq.mm and the latter having a mean of 2600.085 +/- 168.09 cells per sq.mm.

Conclusion: The current study's findings reveal a considerable drop in endothelial cell count in diabetes compared to age-matched controls. Endothelial pleomorphism and hexagonality are observed, although polymegathism is mostly unaffected.

Keywords: Corneal endothelial cell, morphology, patients, diabetes mellitus.

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Introduction

Diabetes mellitus is described as metabolic disorder characterised by chronic Hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. The effects of diabetes mellitus include dysfunction and failure of various organs.[1,2] The prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4%in 2030.The prevalence of diabetes is higher in men than women.[3,4]

According to the recent estimate done by the International Diabetes Federation (IDF), South East- Asia (SEA) Region consisting of India, Sri Lanka, Bangladesh, Bhutan, Mauritius and Maldives, is home to more than 72 million adults with diabetes in 2013 and is Expected to exceed 123 million in 2035. Morbidity and early mortality occur as a result of inadequate healthcare facilities for early detection and initiation of therapy, suboptimal management of diabetes and associated morbidities.[5,6]

All diabetics are at higher risk of developing ocular complications. Diabetes can affect all ocular structures. Abnormal aggregates of collagen fibrils in stromal matrix are common in

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long term. Diabetes, result of excessive non enzymatic glycosylation.5 Diabetic neurotrophic keratopathy is a component of diabetic polyneuropathy.[7]
The corneal endothelial cell damage cause disturbances in the management of Diabetic Retinopathy Pre and Post operatively because the endothelial decompensation can result in bullous keratopathy.[8] Diabetes leads to increased aqueous humour glucose levels and inhibit directly the corneal endothelial function. The recovery rate is slower in diabetics even in euglycemic state. The diabetic patients showed less corneal swelling and reduced corneal recovery from hypoxia when compared to the normal population.[9] The Diabetic corneas were thicker and more auto fluorescent than the non –diabetic corneas. The diabetes mellitus affects the corneal hydration.[10-12]
The endothelial morphology is influenced by many factors. The variants of endothelial morphology i.e., ECD, CV and percentage of hexagonal cells are affected by age, race, and refractive errors. Hence studying the influence of morphological changes due to drugs, devices and diseases are important to control several subject related factors.[13-15]

Aim and objectives
Aim:
Evaluation of the corneal endothelial cells in patients with diabetes mellitus

Objectives
To evaluate endothelial cell count of cornea in patients with diabetes mellitus.
To evaluate morphology of endothelial cells of cornea in patients with diabetes mellitus.

Material and Methods
Place of study: KIMS Hospital, patients coming to Department of General Medicine with diabetes mellitus are evaluated for corneal endothelial cell count and morphology at Department of Ophthalmology
Type of study: Prospective cross sectional and descriptive study
Sample size: patients attending during study period (100) it is calculated according to the sample size calculation formula 4pq/l2
P-prevalence; q-[1-p]; l-allowable error
Study duration: 2 years (October 2018-October 2020)

Inclusion Criteria
- Patients diagnosed with type 1 and type 2 diabetes mellitus.

Exclusion criteria
- Patients with previous h/o ocular surgery
- Patients with previous h/o ocular trauma
- Patients with primary or secondary glaucoma
- Patients with corneal disease
- Dry eye syndrome
- Patients not willing to undergo the study

Study Instruments
- Specular microscopy
- Slit lamp
- Direct Ophthalmoscopy
- Indirect Ophthalmoscopy

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Other Investigations
Blood sugars-

- FBS
- PLBS
- HbA1c

RESULTS

Table 1: Gender Wise Distribution

Groups	Diabetics(n=100)	Percentage	Nondiabetics(n=100)	Percentage
Male	51	51%	53	53%
Female	49	49%	47	47%
Total	100	100%	100	100%

In the present study, in 100 diabetic patients, 51 are males and 49 females. In non-diabetics 53 males and 47 females were included.

Table 2: age wise distribution

	Diabetics(n=100)			Non-Diabetics (n=100)		
Age	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**
41-50	6(11.76%)	6(12.24%)	12(12%)	5(9.43%)	4(8.51%)	9(9%)
51-60	13(25.49%)	10(20.4%)	23(23%)	21(39.62%)	16(34.04%)	37(37%)
61-70	22(43.13%)	22(44.89%)	44(44%)	24(45.28%)	23(48.93%)	47(47%)
71-80	10(19.60%)	11(22.44%)	21(21%)	3(5.66%)	4(8.51%)	7(7%)

The current case control study, included 100 patients of diabetic and 100 patients of non-diabetics. 200 eyes of diabetics and 200 eyes of non-diabetics group were tested and analysed. Male and female population was 51 males and 49 females in diabetic group. 53 males and 47 females in non-diabetic group were included in the study.

Table 3: Endothelial Cell Density in Diabetics and Non-Diabetics

Endothelial Cell Density									
	Diabetics (n=100)				Non-Diabetics (n=100)				
Age	**N**	**Mean**	**SD**	**SEM**	**N**	**Mean**	**SD**	**SEM**	
41-50	12	2617.75	165.704	47.834	9	2807.11	96.586	32.195	p< 0.0001
51-60	23	2452.35	154.895	32.298	37	2590.68	147.471	24.244	
61-70	44	2430.93	282.428	42.578	47	2569.06	181.547	26.481	
71-80	21	2392.10	274.796	59.965	7	2514.00	168.634	63.738	

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In diabetic patients the mean endothelial cell density is 2448.145 +/- 245.77 cells per sq.mm and in non-diabetic 2600.085 +/- 168.09 cells per sq. mm showing the decreased cell density in the diabetic population compared to the non – diabetic control population which is statistically significant ($p < 0.0001$).

Table 4: Age Matched Coefficient of Variation of Endothelial Cells

Age Matched Coefficient of Variation									
	Diabetics(n=100)				**Non-Diabetics(n=100)**				
Age	**N**	**Mean**	**SD**	**SEM**	**N**	**Mean**	**SD**	**SEM**	
41-50	12	37.17	5.060	1.461	9	36.56	4.613	1.538	p Value 0.33
51-60	23	38.22	3.977	0.829	37	38.00	4.955	0.815	
61-70	44	39.55	4.060	0.612	47	38.11	3.164	0.462	
71-80	21	36.67	3.498	0.763	7	36.43	3.867	1.462	

The CV of diabetic eyes was 38.69 +/- 4.23 percent and in non – diabetic eyes 38.285 +/- 4.24 percent which is statistically not significant though the diabetic eyes have marginally higher polymegathism than the non – diabetic eyes.

Table 5: Age Matched Percentage Hexagonality Values of Endothelial Cells.

Age Matched Percentage Hexagonality Values of Endothelial Cells									
	Diabetics (n=100)				**Non-Diabetic (n=100)**				
Age	**N**	**Mean**	**SD**	**SEM**	**N**	**Mean**	**SD**	**SEM**	
41-50	12	43.17	7.346	2.121	9	44.89	4.106	1.396	p < 0.0001
51-60	23	40.70	5.312	1.108	37	43.76	3.804	0.625	
61-70	44	40.32	5.084	0.766	47	43.79	4.525	0.660	
71-80	21	39.48	3.710	0.810	7	42.57	5.127	1.938	

The Hexagonality Percentages of diabetic eyes 40.81 +/- 5.25 percent and non – diabetic 43.595 +/- 4.18 percent with statistical significance ($p<0.0001$) showing the Hexagonality was affected in diabetes mellitus. The decrease in the hexagonality is observed in all age groups.t value is calculated using unpaired t test.

DISCUSSION

Present study consisted of 100 diabetic patients and 100 non diabetic patients with their ages ranging from 41-80 years. These patients were compared of all ages with age matched. These patients were examined in the Topcon SP 3000 P non-contact specular microscope. In all these patients there was decrease in endothelial cell density with age increases in both diabetes and non-diabetes patients. It was studied that loss of endothelial cell count in diabetes patients was significantly more compared with non-diabetic patients. It was also studied that in diabetes mellitus patients there was significant variation in co-efficient of variation and hexagonality of diabetes mellitus compared with non-diabetes mellitus. There was increased co-efficient of variation and decreased hexagonality of endothelial cells in both diabetes and non-diabetes mellitus.[16,17]

Comparison with other studies based on age distribution-

N Buasted etal, in their study included cases from age group of 10-30 years. J.S Lee et ,al., in their study included cases from age of group 8-35 yrs. MM Chooet,al., in their study included cases from the age group 35-80 years. Allan Storr –Paulsen et,al., in their study

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included from the age group 40-70 years. n the present study it was included from age group 41-80 years.[18,19]

Comparison with other studies based on gender distribution-

J.S Lee et,al., in their study they included 53.04% were males and 49.96% were females. Rachapally R Sudhir et al., in their study they included 53.80% were males and 46.20% were females.[20,21]

Rajesh parekh et,al., in their study they included 56.33% were males and 43.67% were females. MM Choo et,al., in their study they included 67% were males and 33 % were females. Beta Urban et al. in their study they included 62% were males and 38% were females. In the present study it was included 100 diabetic patients and 100 non diabetic patients in which there were 52% males and 48% females.[22]

Comparison with other studies based on type of diabetics-

The studies conducted by N Buastedet, al., Beta Urban et, al. included patients with Type 1 diabetes. J.S Lee et, al., included patients with insulin dependent diabetes mellitus. Anna Roszkowaskaet, al., Rajesh Parekh et, al., included both type 1 and type 2 diabetes. MM Chooet, al., Rachapally et, al., Gautham et, al., Allen Storr et, al., included Type 2. The present study included patients with Type 2 Diabetes Mellitus.[19-22]

Comparison with other studies based on number of subjects

The number of subjects in N Buastedet, al., were 81. The number of subjects and controls in J.S. Lee et, al., were 200 and 100. The number of subjects and controls in Anna Roszkowaskaet, al., were 75 and 62. The number of subjects and controls in MM Chooet, al., were 100 and 100. The number of subjects and controls in Beta Urban et, al., were 123 and 124. The number of subjects and controls in Rachapally R Sudhiret, al., were 1191 and 120. The number of subjects and controls in Rajesh Parekh et, al., were 125 and 100. The number of subjects and controls in GauthamKukadiaet, al., were 118 and 100. The number of subjects and controls in Allen Storret, al., were 107 and 128. The number of subjects and controls in Present study are 100 and 100.[15,18,20]

Comparison with other studies based on endothelial cell density

The study conducted by N Buastedet, al., showed that there were no alterations in cell density. The study conducted by J.S. Lee et, al., Anna Roszkowaska et, al., MM Choo et, al.,Beta Urban et, al., Rachapally R Sudhir et, al., Rajesh Parekh et, al., GauthamKukadia et, al., Allen Storr et, al., showed decrease in endothelial cell density. The Present study also shows the decrease in endothelial cell density.[21-23]

Comparison with other studies based on coefficient of varition of endothelial cells

It was observed in study conducted by MM Chooet, al., Rachapally R et, al., Gautham et, al., showed increase in coefficient of variation.

The Present study also showed that there is increase in coefficient of variation.

Comparison with other studies based on hexagonally of endothelial cells

It was observed in study conducted by MM Chooet, al., Rachapally R et, al., showed increase in hexagonality. The study conducted by Gauthamet, al., showed decrease in hexagonality. The Present study also showed that there is decrease in hexagonality.

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Comparison with other studies based on specular microscopes

Maria Letiziasalvetat et,al., In the study conducted compared central corneal thickness and endothelial density with laser scanning confocal microscope Heidelberg Retina tomographyII Rostock corneal Module and noncontact specular microscope Tomey EM-3000 and assessed intra and interobserver agreement in normal corneas mean CCTs with Tomey and HRT were 529.46 +/- 35.4 and 536.6 +/- 37.6 mm (P = 0.06), respectively ;average ECDs with Tomey and HRT were 2473.56 +/- 242.2 and 2539.76 +/- 338.6 cells per square millimetre (P = 0.04), respectively. The mean of the differences (HRT minus Tomey) was 6.5 +/- 6.17 mm for CCT and 65 +/- 135.1 cells per square millimetre for ECD. They concluded HRT II Rostock Corneal Module and the Tomey EM- 3000 showed an overall good inter-method agreement. HRT showed a tendency to slightly overestimate CCT measurements, significantly underestimate ECD measurements in eyes with a reduced cell density (2290 cells per square millimetre), and overestimate ECD in eyes with a high cell density. Both instruments showed low intra- and interobserver TRV for both CCT and ECD measurements, which tended to be less for Tomey.[19]

In the present study Topcon non-contact SP-3000P specular microscope was used. It covers all the needs for endothelial cell analysis and pachymetry with reliable, easy to use functions on broad range and options, it was studied that endothelial cell density of all ages was 2448.145 +/- 0.453 in diabetes.

Comparison of all variables of endothelial cells with age matched diabetes and non-diabetes patients

Variables	Age Group	Diabetics(n=100)	Non diabetics (n=100)	t value	p value
ECD	All ages	2448.145	2600.085	7.21	<0.0001
	41-50	2617.75	2807.11		
	51-60	2452.35	2590.68		
	61-70	2430.93	2569.06		
	71-80	2392.10	2514.00		
CV%	All Ages	38.69	38.265	0.95	0.33
	41-50	37.17	36.56		
	51-60	38.22	38.00		
	61-70	39.55	38.11		
	71-80	36.67	36.43		
Hexagonality	All Ages	40.81	43.595	5.86	<0.0001
	41-50	43.17	44.89		
	51-60	40.70	43.76		
	61-70	40.32	43.79		
	71-80	39.48	42.57		

In diabetic patients the mean endothelial cell density is 2448.145 +/- 245.77 cells per sq.mm and in non-diabetic 2600.085 +/- 168.09 cells per sq. mm showing the decreased cell density in the diabetic population compared to the non – diabetic control population which is statistically significant ($p < 0.0001$).

In the age group of 41-50 the mean endothelial cell density is 2617.75 +/- 165.704 in diabetic group and 2807.11 +/- 96.586 in non-diabetic group. In the age group of 51-60 the mean endothelial cell density is 2452.35 +/- 154.895 in diabetic group and 2590.68 +/- 147.471 in non-diabetic group. In the age group of 61-70 the mean endothelial cell density is 2430.93 +/- 282.428 in diabetic group and 2569.06 +/- 181.547 in non-diabetic group.

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In the age group of 71-80 the mean endothelial cell density is 2392.10 +/- 274.796 in diabetic group and 2514.09 +/- 168.634 in non-diabetic group. The endothelial cell density is maximum in the age group of 41-50 and as the age increases the endothelial cell density decreases. The CV of diabetic eyes was 38.69 +/- 4.23 percent and in non – diabetic eyes 38.285 +/- 4.24 percent which is statistically not significant though the diabetic eyes have marginally higher polymegathism than the non – diabetic eyes. In the age group of 41-50 the coefficient of deviation is 37.17 +/- 5.060 in diabetic group and 36.56 +/- 4.613 in non-diabetic group. In the age group of 51-60 the coefficient of deviation is 38.22 +/- 3.977 in diabetic group and 38.0 +/- 4.955 in non-diabetic group.

In the age group of 61-70 the coefficient of deviation is 39.55 +/- 4.060 in diabetic group and 38.11 +/- 3.164 in non-diabetic group. In the age group of 71-80 the coefficient of deviation is 36.67 +/- 3.498 in diabetic group and 36.43 +/- 3.867 in non-diabetic group. The observation made from the above data is, as the age increase the coefficient of variation increases.

The Hexagonality Percentages of diabetic eyes 40.81 +/- 5.25 percent and non – diabetic 43.595 +/- 4.18 percent with statistical significance ($p<0.0001$) showing the Hexagonality was affected in diabetes mellitus. The decrease in the hexagonality is observed in all age groups. In the age group of 41-50 the hexagonality percentages is 43.17 +/- 7.346 in diabetic group and 44.89 +/- 4.106 in non-diabetic group. In the age group of 51-60 the hexagonality percentages is 40.70 +/- 5.312 in diabetic group and 43.76 +/- 3.804 in non-diabetic group.

In the age group of 61-70 the hexagonality percentages is 40.32 +/- 5.084 in diabetic group and 43.79 +/- 4.525 in non-diabetic group. In the age group of 71-80 the hexagonality percentages is 39.48 +/- 3.710 in diabetic group and 42.57 +/- 5.127 in non-diabetic group.

The hexagonality percentage decreases as the age increases.

CONCLUSION

In diabetes eyes, the endothelium is under metabolic stress, which leads to decrease in cell density and altered function of the endothelium. The corneal endothelium regulates the corneal hydration and plays an important role maintaining the corneal transparency. Any change in the morphology of the endothelium is reflected in its function and regulation of hydration of the cornea. The results of present study suggest that the endothelial cell count is significantly decreased in diabetes compared with the age matched controls. The altered endothelial morphology seen in the form of pleomorphism and hexagonality but polymegathism is not significantly altered. Diabetes is a chronic metabolic disease and it is common to have some association between the systemic and ocular factors influencing the corneal endothelium. Precautionary measures have to be taken in diabetics before any intra-ocular-procedures, prolonged period of contact lens wear, in glaucoma and use of drugs that affect the endothelium.

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