 DOI: 10.18231/2395-1451.2017.0038

Comparison of endothelial cell characteristics and corneal thickness between diabetics and non-diabetics

Minu Ramakrishnan[1], Saba Kausar[2,*], Mayur Agarwal[3]

[1]Professor & HOD, [2,3]Senior Resident, Dept. of Ophthalmology, KJ Somaiya Hospital, Maharashtra

***Corresponding Author:**
Email: kausarsaba31@gmail.com

Abstract

Objectives: To compare endothelial cell characteristics & corneal thickness between diabetic and non-diabetic population.

Materials and Methods: This was a prospective, non-interventional, cross sectional study where 200 consecutive patients with diabetes mellitus and 100 controls were examined. Complete medical history was taken and ophthalmologic examination was done, including best corrected visual acuity tested by Snellen's chart, intraocular pressure using applanation tonometer, slit-lamp examination, endothelial cell count and morphology (using non-contact specular microscopy) and central corneal thickness and binocular indirect ophthalmoscopic fundus examination. Patients with diabetic retinopathy were graded according to Early Treatment Diabetic Retinopathy Study (ETDRS) study. Data obtained was grouped and analysed.

Results: The mean endothelial cell count in diabetic group was significantly lesser than that in the control group. (p=0.000). Also a reduction in the mean percentage of hexagonal cells was seen in diabetic group. (p=0.000)

Whereas the mean corneal thickness in diabetic group was found to be more than that in the control group. (p=0.000). And we also found that there was a significant increase in the mean coefficient of variation in diabetic group as compared to control group.(p=0.000)

Conclusion: The mean endothelial cell count is significantly lower in diabetics as compared to non-diabetics. The mean corneal thickness and also the mean coefficient of variation in diabetics is higher than the non-diabetics, but the mean percentage of hexagonal cells in diabetics is reduced.

Keywords: Corneal thickness, Endothelial cell count, Diabetic, Non-diabetic.

Introduction

Diabetes mellitus is a very frequent disease worldwide, having a considerable impact on society, not only due to its high prevalence but also because of its chronic complications and high mortality rate.[1,2] In 2010 , it was estimated that 6.4% of the world's adult population, live with diabetes. The number is expected to grow to 7.8% of the adult population by 2030.[3]

The largest age group currently affected by diabetes is between 40-59 years. By 2030 this is expected to move to the age group of 60-79 years.[3] Seventy percent of the current cases of diabetes are seen in the developing countries. With an estimated 50.8 million people living with diabetes, India has the world's largest diabetes population.[3] Diabetes (type 1 and 2) is found in 13% of patients over 60 years of age.[4]

Diabetes mellitus is the leading cause of blindness in adults between the age of 20 to 74 years and can affect almost every ocular structure. It has been estimated that patients with diabetes are 25 to 30 times more likely to lose their vision than persons of similar age who are not diabetic.[5,6] Diabetes is an enormous public health problem, not only because it can lead to ophthalmic complications, but also because of the neurological and vascular sequel.[7] For many patients, timely intervention can substantially reduce the likelihood of blindness.[7] Early diagnosis of diabetes allows education of the patient and starting on adequate treatment and thus avoiding potential complications, which is a root cause in development of this disease.

At the ocular level, it causes diabetic retinopathy, cataracts[3] and glaucoma;[8] diabetic retinopathy being the most frequent cause of blindness in the working age individuals and second cause of blindness after ARMD (age related macular degeneration).[9] Diabetic keratopathy is a frequent disease wherein several alterations are seen, especially in epithelium and endothelium. Alterations in the endothelium result in a deficient pumping function and possibly endothelial thickening and folds.

The occurrence of dry eye disease and other ocular surface diseases has also increased in diabetic patients.[10] Studies were conducted in southern India[11]which showed that the cornea and the ocular surface underwent structural and functional changes which could be quantified, but there is no study based on data from western India. The purpose of this study is to determine the corneal function (cell count and thickness) and corneal cell morphology (pleomorphism and polymegathism) in diabetics and non-diabetics in our population.

Materials and Methods

After taking institutional review board and ethics committee approval, we conducted this prospective study, where we examined 200 consecutive patients with diabetes mellitus and 100 controls who attended the ophthalmology outpatient department of a private

charitable medical college hospital in Western India, over a period of two years from April 2010 to April 2012. Sample size was estimated by a pilot study undertaken in the department to assess burden of disease in population and evidence of significant changes in cell count and corneal thickness in patients and controls. The age of diabetic and control group ranged between 30 – 70 years. Both groups were age and sex matched. Informed consent was taken from both study and the control group. Ophthalmologic examination included a complete systemic history, visual acuity using Snellen's chart, slit-lamp examination, applanation tonometry by Goldmann applanation tonometer, binocular indirect ophthalmoscopic fundus examination and endothelial cell count and morphology (using non-contact specular microscopy) and central corneal thickness. Those patients diagnosed with diabetic retinopathy were evaluated by a retina specialist who classified diabetic retinopathy and decided further line of management. Diabetic Retinopathy was graded according to Early Treatment Diabetic Retinopathy Study (ETDRS) study. Retinal status was evaluated by indirect ophthalmoscopy after dilation by Tropicamide eye drops and retinal colour photography taken and angiography done as required.

Specular microscopy of both the eyes, examining the central corneal endothelium was done using a specular microscope (Konan KSS 400). Using the 'dot' method, 100 cells were digitalized by touching the cell apices with a graphic tablet pen, and the cell sizes were analysed for a variety of factors that included endothelial cell density, the percentage of hexagonal cells and the coefficient of variation of cell area (SD/mean). Specular microscopy also provided the corneal thickness by optical pachymeter principle. All data were recorded by a single skilled observer by taking 3 photographs for analysis.

Controls were selected by evaluating their fasting and post prandial blood sugars which were within normal limits, and complete examination was performed similar to cases.

All the statistical tests and analyses were based on average of data from both eyes. SPSS software was used for analysis. Quantitative data was represented as mean and standard deviation (SD). ANOVA and Kruskal Wallis test were conducted on mean and SD values to arrive at p values. P value <0.05 was considered significant.

Patients with history of ocular disease, corneal opacities or dystrophy, any surgical intervention, contact lens wear or on topical ocular medications were excluded from both the groups.

Results

The mean endothelial cell count in diabetic group was lesser as compared to the control group. (p=0.000) Within the diabetic group, we found that the mean endothelial cell count was significantly reduced in severe NPDR and PDR patients. We also found it to be significantly low in patients with diabetes of more than ten years duration and in patients more than 50 years of age.

The mean corneal thickness in diabetic group was more than that in control group. (p=0.000). Among the diabetic group, we observed that the mean corneal thickness was significantly increased in severe NPDR and PDR patients. We also found it to be significantly increased in patients with diabetes of more than ten years duration and in patients more than 60 years of age.

We also found that the mean coefficient of variation in diabetic group was more than that seen in control group. (p=0.000) But the mean percentage of hexagonal cells in diabetic group was lesser as compared to that in control group. (p=0.000)

Discussion

Our study included 200 diabetics and 100 controls to assess and compare the corneal function (cell count and thickness) and morphology (cell size and shape) in the two groups. Detailed age and sex data of the patients is presented in Table 1.

Our study showed that there was a significant decrease in the mean endothelial cell count in diabetics over controls. (p = 0.000). (Table 2)When the cell count was studied according to severity of diabetic retinopathy, our study showed that the cell count was significantly decreased in patients with severe NPDR and PDR. (p< 0.05)(Table 3 a)

It also showed that cell count was reduced in patients above 50 years of age and those with diabetes of more than 10 years duration. (p< 0.05) Lee et al[12] who worked on a similar study in Korea reported that the diabetic patients had lesser cell density (p < 0.05). The endothelial cell density was lower for patients suffering from diabetes for more than 10 years duration than those suffering from it for less than 10 years duration (P < 0.05). Parekh et al,[15] who conducted a similar study in Bangalore, observed that duration of diabetes has a significant correlation with decrease in cell density (p < 0.0001). They also found decrease in cell count according to severity of diabetes. (p< 0.0001)(Table 3b and 3c)

When corneal thickness was compared in both the groups, we found that there was statistically significant increase in the corneal thickness in the diabetic group as compared to the non-diabetic group. (p = 0.000). When corneal thickness was studied according to severity of diabetic retinopathy, we found that the corneal thickness was significantly high in severe NPDR and PDR patients. (p< 0.05) Our study also showed that corneal thickness increased in patients above 50 years of age and those who were having diabetes of more than ten years of duration. (p< 0.05) (Table 3)

Lee et al[12] reported that the diabetic patients had thicker cornea than controls (P < 0.05). Corneal thickness was significantly higher for diabetics of more than ten years duration than for diabetics of less than 10 years duration (P < 0.05). Busted et al[14] showed that the diabetic corneal thickness was significantly thicker than the normal corneal thickness, but they did not find any significant relation between central corneal thickness of diabetes and the diabetic duration. Parekh et al[15] observed that duration of diabetes had significant correlation with increase in cell thickness (p < 0.0001). They also found increase in thickness according to severity of diabetes. (p< 0.0001)

This change in corneal function is probably due to increased levels of aldose reductase activity in both the epithelium and endothelium. Corneal oedema may result from an abnormally high level of sorbitol in the endothelium, which interferes with the sodium-potassium adenosine triphosphatase (ATPase) pump.

Polymegathism is one of the early signs of endothelial disease, characterised by abnormal variation in the shape of endothelial cells and it also reflects an abnormal rate of endothelial wound repair. Coefficient of Variation represents the degree of polymegathism.

In our study when we compared coefficient of variation in both the groups we found that there was significant increase in coefficient of variation in diabetic group over controls. (p = 0.000) The coefficient of variation was 42.19 in diabetic and it was 37.15 in controls. (Table 2)

Pleomorphism which is another early sign of endothelial disease, is characterised by abnormal variation in the shape of the endothelial cells representing structural inability of the endothelium. The degree of pleomorphism is represented by 6A measurements. (Percentage of hexagonal cells.)

In our study, when we compared percentage of hexagonal cells in between the two groups, we observed that there was statistically significant decrease in the percentage of hexagonal cells in diabetic group. (p = 0.000) (Table 2)

Lee et al[12] reported that the diabetic patients had lesser hexagonality and more irregular cell size of the corneal endothelium than did the controls (P < 0.05). The coefficient of variation of cell size were significantly higher in diabetics of more than ten years duration than in diabetics of less than ten years duration (P < 0.05). Also the percentage of hexagonal cells were lower for diabetics of more than ten years duration than in diabetics of under ten years (P < 0.05). Keoleian et al[13] who worked on a similar study in New York reported that diabetic patients often had abnormal corneal endothelium in contrast to normal persons, but there was no significant difference in terms of function of the fluorescence permeability of the corneal thickness and endothelium. Thus implying that the corneal endothelium of diabetic patients had a structural disorder, but the function of the corneal tissues is not affected. Parekh et al[15] observed significant pleomorphism and polymegathism. (p< 0.0001)

Thus results of our study were in accordance to the above studies done in other parts of the world. In our study we did not assess corneal sensations as corneal aesthesiometer was not available. Also there is scope for further research relating to corneal and ocular surface changes in diabetic patients.

Special care is to be taken during ocular surgeries in case of diabetic patients as there may be corneal endothelial and ocular surface changes in these patients. One may have to use dispersive viscoelastic agents to protect the endothelium in diabetic patients. Also, increase in tissue in thicker cornea makes it less compliant and subsequently leading to overestimation of intraocular pressure (by Goldmann applanation tonometer). These justify the need for undertaking further research on this topic, and taking due precautions as necessary.

Table 1: Age and sex wise distribution of diabetic and control group

Age	DM	No DM	P value
Mean	50.44	50.17	0.840 (Unpaired T test)
SD	9.03	9.87	
Sex			
Males	104(52%)	50 (50%)	0.777 (Pearson Chi Square test)
Females	96(48%)	50 (50%)	

Table 2: Comparison between cell density, corneal thickness, coefficient of variation, percentage of hexagonality between diabetics and non-diabetics

Parameter	DM	No DM
Cell Density	2,684.44	2,945.22
Corneal Thickness	566.55	533.70
Coefficient of Variation	42.19	37.15
% of Hexagonality	43.73	47.08

DM: Diabetes Mellitus

Table 3: Comparison of cell density and corneal thickness with a) severity of diabetes b) age and c) duration of diabetes

	Cell density			Corneal thickness		
a) Severity of diabetes (ETDRS)	**Mean**	**SD**		**Mean**	**SD**	
Mild to Moderate NPDR	2,740.09	182.50		557.30	18.63	
Sever NPDR	2,538.79	177.59		594.50	21.67	
PDR	2,452.69	83.16		595.58	9.30	
WNL	2,850.00	235.32		546.83	10.02	
b) Age wise distribution						
Less than 40 Yrs.	2,853	141		551	15	
41 to 50 Yrs.	2,697	203		563	22	
51 to 60 Yrs.	2,643	204		570	23	
More than 60 Yrs.	2,536	213		589	32	
c) Duration of diabetes						
Less than 1 Yr.	2,930	173	P value <0.001 (ANOVA test)	552	7	P value <0.001 (Kruskal Wallis test)
1 to 5 Yrs	2,743	184		560	18	
5 to 10 Yrs	2,625	204		567	25	
More than 10 Yrs	2,576	189		586	29	

ETDRS: Early Treatment Diabetic Retinopathy Study; NPDR: Non-proliferative diabetic Retinopathy; PDR: Proliferative Diabetic retinopathy; WNL: Within normal limits

References

1. Goday A. Epidemiology of diabetes and its non-coronary complications. Rev EspCardiol 2002;55:657-670.
2. Kothari V, Stevens RJ, Adler AI, Strattton IM, Manely SE, Neil HA, et al. UKPDS 60: risk of stroke in type 2 diabetes estimated by the UK Prospective Diabetes study risk engine. Stroke 2002;33:1776-1781.
3. Source: IDF, Diabetes Atlas, 4th edition. (last updated 15 March 2012).
4. Gupta HL, Yadav M, Sundarka M K, Talwar V, Saini M, Garg P. A study of prevalence of health problems in asymptomatic elderly individuals in Delhi. J Assoc Physicians India 2002;50:792-795.
5. Bourne WM. Biology of the corneal endothelium in health and disease. Eye 2003,Nov;17(8):912-8.
6. Javitt JC, Canner JK, Frank RG et al: Detecting and treating retinopathy in patients with type I diabetes mellitus: a health policy model. Ophthalmology 97:483,1990.
7. Fernandez-Vigo Lopez J. Diabetes Ocular. Barcelona: EDIKA-MED;1992.
8. Honrubia Lopez FM. Ophthalmologia General; 2002.
9. Ramos-Remus C, Suarez-Almazor M, Russell AS: Performance of on line biomedical databases in rheumatology. ClinExpRheumatol 1994,12(4):375-80.
10. Lemp MA: Report of The National Eye Institute/Industry Workshop on clinical trials in dryeyes. CLAO1995,21(4):221-232.
11. Lemp MA. Contact lenses and allergy. CurrOpin Allergy ClinImmunol. 2008;8:457-460.
12. JS Lee, BS Oum, HY Choi, JE Lee and BM Cho. Differences in corneal thickness and corneal endothelium related to duration in Diabetes. Eye (2006)20,315–318.
13. Keoleian GM, Pach JM, Hodge DO, Trocme SD, Bourne WM. Structural and functional studies of the corneal endothelium in diabetes mellitus. Am J Ophthalmol 1992;113:67–70.
14. Busted N, Olsen T, Schmitz O. Clinical observations on corneal thickness and the corneal endothelium in diabetes mellitus. Br J Ophthalmol 1981;65:687–690.
15. Rajesh Parekh, K.N. Ranganath, K.P. Suresh, Mala Dharmalingam. Corneal endothelium in diabetes. Int J DiabDevCtries March 2006;Vol 26:24-26.