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Central Corneal Thickness in Type 2 Diabetic Patients And its Correlation with Duration , Hba1c Levels And Severity of Retinopathy.

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Abstract: *The purpose of our study was to compare the central corneal thickness(CCT) in type 2 diabetes mellitus (T2DM)patients with age and sex matched healthy controls and to analyze it's association with HbA1c, duration of disease and severity of retinopathy. Methods: The study was conducted on 120 eyes each of T2DM patients and normal age and sex matched non diabetic controls. After recording age, sex, duration of diabetes and HbA1c level, specular microscopy, pentacam examination, and fundus examination was done. CCT was then correlated with endothelial cell density(ECD),HbA1c ,duration of diabetes and severity of retinopathy. Results: In the diabetic group, the mean CCT (565.32±34 μm) and mean ECD (2489± 508 cells/mm 2), varied significantly from non diabetic controls with mean CCT(532 ±30.7 μm) (P=0.00001) and mean ECD 2679± 498 cell/mm2. (P=0.0008), CCT was significantly thicker for diabetics with duration of >10 years than with <10 years (P=0.015). and with HbA1c >7 than HbA1c <7.(p=0.00001)CCT was thicker for diabetics with diabetic retinopathy compared to those with no retinopathy but was not statistically significant(p=0.13)In conclusion, subjects with type 2 DM exhibit significant increase in CCT which is correlated with ECD,disease duration and HbA1c levels and not with severity of retinopathy.*

Key-words : *central corneal thickness – corneal endothelial cells – controls -diabetes mellitus type II – duration*

I. Introduction

Diabetes mellitus (DM) continues to be a tremendous health burden in the world affecting about 415 million adults which is likely to reach 642 million in 2040.[1] It is characterized by hyperglycemia and development of micro and macrovascular changes leading to morphological and functional changes in different organs. Like any other organ diabetes affects every tissue of eye .The most prominent complications being diabetic retinopathy, neovascular glaucoma, changes of refractions, and cataract progression. Anatomical and physiological changes occur in every part of cornea including epithelium,endothelium and stroma. Initial studies by Busted et al. and Schultz et al. [2,3] reported increased polymegethism , polymorphism with increased central corneal thickness (CCT) and normal endothelial cell density (ECD) though recent studies by Roszkowska et al., Inoue et al., Lee et al .,concluded that there was also decreased ECD along with other morphological changes which subsequently decrease endothelium function, causing corneal hydration and increase central corneal thickness.[4,5,6] Like in retina, kidney or any other organ, in cornea also functional abnormalities may be detected much before any symptom or clinically evident lesion appears.Increased corneal thickness is considered to be one of the earliest clinically detectable changes of the diabetic eye.[2] Central corneal thickness (CCT) is an important parameter for the evaluation of suitable patients for refractive surgery, when assessing glaucoma risk and evaluating physiological and pathological variations of the corneal structure[7]

The aim of our current study was to compare the central corneal thickness in type 2 diabetes mellitus patients with age and sex matched healthy controls and also to analyze it's association with HbA1c, duration of disease and severity of retinal disease.

II. Material And Methods

The study was conducted on 240 eyes, 120 of which were of Type 2 diabetes mellitus(T2DM) patients and 120 eyes of normal age and sex matched non diabetic controls. Right eye of every individual was studied and left eye was taken up in case of any disease in right eye. Individuals with history of ocular infection, inflammation, trauma, surgery or photocoagulation were excluded from the study. Diagnosed cases of glaucoma

and individuals putting any eye drops or using contact lenses were also not included. Informed consent of each patient was taken and age , sex, duration of diabetes and latest HbA1c level was recorded . After recording the visual acuity and detailed examination on slit lamp patient was subjected to specular microscopy, pentacam examination, IOP measurement and fundus examination. Specular microscopy was done using non-contact Topcon SP-3000P (Topcon Corp, Tokyo, Japan) specular microscope.60+/-10 endothelial cells were counted in each image .This was repeated three times and the image with median number of endothelial cells was used for analysis and ECD was recorded. CCT was measured using Pentacam HR tomographer (Oculus, Wetzlar,Germany) with rotating scheimpflug camera and mean of three readings was recorded. IOP measurement was done using Goldmann application tonometer. All CCT and IOP recordings were done between 12 -2 pm keeping in mind diurnal variations. Fundus examination was done using +90D lens and based on Early Treatment of Diabetic Retinopathy Study (ETDRS),patients were classified and divided into three groups . Group 1 with no diabetic retinopathy, Group 2 with non-proliferative diabetic retinopathy and Group 3 with proliferative diabetic retinopathy. Central corneal thickness(CCT) was then correlated with endothelial cell density(ECD), HbA1c ,duration of diabetes and severity of retinopathy.

III. Observations

Out of total 240 individuals enrolled in the study 120 were type2 diabetic patients and 120 age and sex matched normal controls.Their demographic and clinical status are tabulated in Table 1.

Table 1: Demographic and clinical characteristics of patients with II diabetes mellitus.

	Diabetics n=120	non diabetics n=120	p value
age in years	53.5±5.5	52.8 ±6.2	
males	72	69	
females	58	59	
mean HbA1c	9.3±2.1	5.5±1.2	
duration of diabetes(years)	12.3±7.5 (1-25)		

Diabetic patients and non diabetic controls were age and sex matched.

Table 2 : Corneal parameters of diabetics and controls

corneal parameters	Diabetics (1n=20)	non diabetics (n-120)	p value
endothelial cell count	2489±508cells/mm2	2697±-498cells/mm2	0.0008
central corneal thickness(μm)	565.32±34.3	532.6±30.7	0.00001
intraocular pressure(IOP)	16.53±1.2	15.4±4.3	

Corneas of diabetic patients showed significant decrease in ECD and increase in central corneal thickness as compared to non diabetics. Diabetics recorded higher IOP. Table 2

Table 3 Variation of CCT (μm)with duration of diabetes

Duration of diabetes	number of patients	CCT (μm)	ECD(cell/mm)	IOP(mmHg)
<10 YEARS	68	554.4±79	2503±302	16.2±1.2
>10 YEARS	52	576.3 ±21.	2456±98	16.7±2.3

Central corneal thickness in a group with diabetic duration >10 years was significantly higher than in patients with diabetic age <10years (p =0.015)

Table 4 : Variation of CCT with HbA1c level

HbA1c level	Mean age	CCT (μm)	ECD (cells/mm2)	IOP(mmHg)
<7	53.2±4.5	548±11.9	2519±343	16.31±1.5
>7	51.67±5.3	561±9.5	2430±345	16.35±2.1

Uncontrolled diabetics had lower ECD , higher IOP and significantly thicker corneas. (p=0.00001)

Table 4. Central corneal thickness (μm) values increased from patients with no diabetic retinopathy to those with proliferative retinopathy but the increase was not statistically significant. (p= 0.13)

Group	N	Central corneal thickness(CCT)
group1 (NDR)	64	566.1± 13.35
group (NPDR)	47	569.4±15.04
group3(PDR)	9	575.1±12.54
controls	120	532.6±30.7

Table 5. Intraocular pressure (mmHg) in groups.

Groups	number of patients(N)	intra ocular pressure(IOP)	central corneal thickness(CCT)
Group 1	64	16.1±3.5	566.1±13.35
Group 2	47	16.7±2.1	569.4±15.04
Group 3	9	16.5±1.2	575±12.54
Controls	120	15.4±4.3	532±30.7

Mean Intraocular pressure was highest in patients with proliferative diabetic retinopathy and least in controls without diabetes but increase was not statistically significant (p=0.12)

IV. Discussion

Central corneal thickness is an important indicator of corneal health status and a key parameter for refractive surgery and estimation of IOP. Diabetic patient's central corneal thickness is greater than non diabetics . Pathogenesis of which is not very well understood and various hypothesis have been put forward. It may be due to structural and functional changes in corneal endothelium as reported by McNamara et al [8] ,Weston et al [9] and Su et al [10] who suggested that hyperglycemia alters endothelial structure leading to hydration of cornea and hence increased corneal thickness. where as Lopez et al concluded that diabetics exhibited increase in CCT due to greater pleomorphism and polymegatism in their corneas.[11] In contrast Busted et al found that the augmented corneal thickness was present early in the disease probably due to corneal dysfunction but much before any visible structural change in the endothelium .[2] Collagen crosslinking may be another reason leading to increase in corneal thickening and gradual stiffening of the cornea that consequently affect the accuracy of IOP measurements [12]

In the present study we found a mean CCT of 565.32 μm ± 34.3 and 532.6 μm ± 30.7 μm in diabetics and non diabetics respectively and this difference was statistically significant. Increase in CCT was significantly correlated with ECD ,degree of hyperglycemia and duration of diabetes .There was definite increase in CCT in patients with severity of retinopathy than in patients without retinopathy but it was not statistically significant. Controls without diabetes showed lower values of IOP than patients with diabetes but again the correlation was not statistically significant. Increase in CCT in diabetic patients in our study was supported by Roszkowska et al [5],lee et al [4] Beata Urban et al[13]and Stella Briggs[14] who reported significantly thicker corneas and decreased ECD, decreased hexagonality and increased CV in diabetics. Larson et al [15] and McNamara et al [8] recorded similar changes in type 1 diabetics . Busted et al[2] and Weston et al [9] also recorded increased CCT but with no effect on ECD and CV. However, a study conducted by Schultz et al[3] Inoue et al [6] and Weimer et al [16] found no differences in the CCT measurements between diabetic and healthy subjects though Inoue et al exhibited decreased ECD and increased CV, Schultz et al found normal ECD, increased CV and Weimer et al no change in endothelium morphology.

Similar to our study McNamara et al in Type 1 diabetics [8] Busted et al [2] Su et al [10] and Yasgan S et al [17] observed positive correlation between HbA1c level and CCT whereas McNamara et al in Type 2 diabetics ,Wiemer et al [16] Ozdamar et al[18] Choo et al [19]and Beata Urban et al[13] did report thicker corneas in diabetics but found no direct correlation with HbA1c levels. Diabetic patients in the present study showed significant increase inCCT compared with normal persons and it was found to be more thick in diabetics with duration> 10 years .This observation was reinforced by Lee et al [4] Beata Urban [13] and Sribunku et al [20] .Though Ozdamar et al.[18] and Stella Briggs et al [14] also interpreted significantly increased CCT in diabetic patients but rejected it's correlation with duration of diabetes.

Possible explanation for increased CCT in diabetics include increased endothelial permeability and increased stromal swelling pressure due to accumulation of sorbitol or from glycosylation of corneal collagen [21] All these mechanisms seem to affected with ECD, endothelial morphology ,glycemic control and duration of diabetes thus supporting our observations .

Ozdamar et al[18] Choo et al[19]reported in their studies that patients with proliferative retinopathy had thicker CCT than those with nonproliferative retinopathy and no retinopathy; however, the difference was not statistically significant.This was similar to our observations.More recent studies by Toygar et al [22]and Mathebula et al [23]were also in agreement with the previous studies.Busted et al.[2] and Wiemer et al.[16] found that CCT increased in DM regardless of the severity of the retinal disease .Stella B et al observed that Type 2 diabetics exhibited significant changes in ECD, IOP and CCT, which, however, were not correlated with disease duration .This finding was consistent with previous studies [17,24,25] Scheler et al [26]and Yasgan S et al [17] found that increases in IOP were closely related to HbA1C levels . In the present study similar to a recent study by Toygar et al. where mean IOP was higher in diabetic patients than in controls; however, the difference was not significant (P = 0.061).

Limitations We recorded only ECD and not hexagonality and CV to assess the correlation between the CCT and the morphology of endothelium .Secondly we did not exclude the patients with dry eye disease which is another important cause of increased corneal thickness.

V. Conclusions

The corneas of Type 2 diabetics were significantly thicker, had lesser endothelial cell density and recorded higher though not statistically significant intra ocular pressure. Central corneal thickness was significantly correlated with duration of diabetes and HbA1c level . CCT increased with grades of retinopathy but was not statistically significant.Routine assessment of CCT and corneal endothelial structure may be beneficial in all diabetic patients along with their usual retinopathy assessment to prevent visual disability by early detection and management.

References

[1]. International Diabetes Federation Diabetes atlas, third ed Brussels. 2006. www.eatlas.idf.org.
[2]. Busted N., Olsen T. and Schmitz O. (1981).Clinical observations on the corneal thickness and the corneal endothelium in diabetes mellitus. Br. J. Ophthalmol. 65, 687-690.
[3]. Schultz R.O., Matsuda M., Yee R.W., Edelhauser H.F. and Schultz K.J. (1984). Corneal endothelial changes in type I and type II diabetes mellitus. Am. J. Ophthalmol. 98, 401-410.
[4]. Lee JS, Oum BS, Choi HY, Lee JE & Cho BM (2006): Differences in corneal thickness and corneal endothelium related to duration in diabetes. Eye 20: 315–318.
[5]. Roszkowska AM, Tringali CG, Colosi P, Squeri CA & Ferreri G (1999): Corneal endothelium evaluation in type I and type II diabetes mellitus. Ophthalmologica 213: 258–261.
[6]. Inoue K, Kato S, Inoue Y, Amano S & Oshika T (2002a): The corneal endothelium and thickness in type II diabetes mellitus. Jpn J Ophthalmol 46: 65–69.
[7]. Gros-Otero J, Arruabarrena-Sanchez C, Teus M. Central corneal thickness in a healthy Spanish population. Arch Soc Esp Oftamol. 2011;86:73–76. PMID: 21511100, http://dx.doi.org/10.1016/j.oftal.2010.12.008
[8]. McNamara NA, Brand RJ, Polse KA, Bourne WM. Corneal function during normal and high serum glucose levels in diabetes. Invest Ophthalmol Vis Sci 1998; 39: 3-17.
[9]. Weston B.C., Bourne W.M., Polse K.A. and Hodge D.O. (1995). Corneal hydration control in diabetes mellitus. Invest. Ophthalmol. Vis. Sci. 36, 586-595.
[10]. Su D.H., Wong T.Y., Wong W.L., Saw S.M., Tan D.T., Shen S.Y., Loon S.C., Foster P.J., Aung T. and Singapore Malay Eye Study Group. (2008). Diabetes, hyperglycemia, and central corneal thickness: the Singapore Malay Eye Study. Ophthalmology 115, 964-968
[11]. López Alemany A. Lentes de Contacto: Materiales y Aspectos Clínicos. Barcelona: Edicions ULLEYE; 1997.
[12]. Kruger RR, Ramos-Estaban JC. How might corneal elasticity help us understand diabetes and intraocular pressure? J Refract Surg 2007; 23: 85–88.
[13]. Beata Urban et al Evaluation of Corneal Endothelium in Children and Adolescents with Type 1 Diabetes Mellitus Mediators Inflamm. 2013; 2013: 913754. doi: 10.1155/2013/913754
[14]. Stella Briggs et al Manifestations of type 2 diabetes in corneal endothelial cell density, corneal thickness and intraocular pressure J Biomed Res. 2016 Jan; 30(1): 46–51.
[15]. Larsson L.I., Bourne W.M., Pach J.M. and Brubaker R.F. (1996). Structure and function of the corneal endothelium in diabetes mellitus type I and type II. Arch. Ophthalmol. 114, 9-14.
[16]. Wiemer NG The influence of chronic diabetes mellitus on the thickness and the shape of the anterior and posterior surface of the cornea.Cornea. 2007 Dec;26(10):1165-70.
[17]. Yazgan S, Celik U, Kaldırım H, et al. Evaluation of the relationship between corneal biomechanic and HbA1C levels in type 2 diabetes patients[J] Clin Ophthalmol. 2014;8:1549–1553.
[18]. Ozdamar Y et al Is there a correlation between diabetes mellitus and central corneal thickness?J Glaucoma. 2010 Dec;19(9):613-6. doi: 10.1097/IJG.0b013e3181ca7c62 19
[19]. MM Choo et al Corneal changes in type II diabetes mellitus in Malaysia
[20]. Int J Ophthalmol. 2010; 3(3): 234–236. Published online 2010 September 18. doi: 10.3980/j.issn.2222-3959.2010.03.12
[21]. Siribunkum J., Kosrirukvongs P. and Singalavanija A. (2001). Corneal abnormalities in diabetes. J. Med. Assoc. Thai. 84, 1075-1083.
[22]. O'Donnell C, Efron N, Boulton AJM. A prospective study of contact lens wear in diabetes mellitus. Ophthalmic and Physiological Optics.2001;21(2):127–138
[23]. Okan T et al Central corneal thickness in type II diabetes mellitus: is it related to the severity of diabetic retinopathy? Turk J Med Sci(2015) 45: 651-654doi:10.3906/sag-1404-153
[24]. Solani D. Mathebula et al Is the central corneal thickness of diabetic patients thicker than that of non-diabetics' eyes?African Vision and Eye Health; Vol 74, No 1 (2015), 5 pages. doi: 10.4102/aveh.v74i1.307
[25]. Zhao D, Cho J, Kim MH, et al. Diabetes, Fasting Glucose, and the Risk of Glaucoma: A Meta-analysis[J] Ophthalmology. 2014 doi: 10.1016/j.ophtha.2014.07.051.
[26]. Chopra V, Varma R, Francis BA, et al. Type 2 diabetes mellitus and the risk of open-angle glaucoma the Los Angeles Latino Eye Study[J] Ophthalmology. 2008;115:227–232
[27]. Scheler A, Spoerl E, Boehm AG. Effect of diabetes mellitus on corneal biomechanics and measurement of intraocular pressure. Acta Ophthalmol. 2012;90(6):447–451