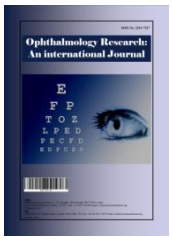

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A Study of Corneal Thickness in Type 2 Diabetes Mellitus with and without Diabetic Retinopathy

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Author's contribution

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Background: It is essential to assess the corneal thickness in diabetes patient.
Introduction: diabetes mellitus is a major cause of blindness throughout the worldDiabetic retinopathy is the most importance given on day to day basics studies especially for ophthalmologist studied indicators in eye. However, functional oddities have been recognised in cornea too like changes in central corneal thickness.
Objectives: 1. To estimate the central corneal thickness (CCT) of type 2 diabetes mellitus patients without diabetic retinopathy age/sex matched normal people. 2. To measure central corneal thickness (CCT) of type 2 diabetes mellitus patient with diabetic retinopathy with age/ sex matched normal person.
Methods: This is a hospital based case control study.
Expected Results: The central corneal thickness is more in type 2 diabetes patients than non-diabetic individual.

Keywords: Specular microscopy; endothelial cell count; diabetes; central corneal thickness diabetic retinopathy.

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1. INTRODUCTION

Diabetes mellitus is considered a foremost non-communicable disease worldwide based on estimate worldwide by international diabetes federations, 80% of new cases are expected to occur in the developing world and in India diabetic population is expected to twofold by year 2030.

Diabetes mellitus (DM) is a worldwide pandemic disease. As of 2010, more than 200 million people had been diagnosed with diabetes and this number is predicted to increase by 62% by 2025 [1].

Diabetic Retinopathy (DR) is one of the major microvascular complication of type 2 diabetes mellitus (T2DM) that is responsible for irreversible blindness among DM patients all over the world [2].

A symbol of DR is adaptations of blood-retinal barrier that is depicted by pericyte loss and breakdown of endothelial cell junction [3]. Corneal abnormalities due to DM might appear or become exacerbated following trauma and different surgeries of retina, cataract, or refractive surgery [4].

Endothelial cell of cornea is responsible for preserving the transparency of the cornea. There is narrow ability of mitosis in endothelium of cornea and once injured, remaining cells widen up to cover up the damaged area. There will be increase in variation of cell area called polymegathism or coefficient of variation and index or pleomorphism.

Central corneal thickness (CCT) can be used as a marker to assess of endothelial health and can be used to evaluate the corneal edema in future perspects of corneal injury. There is hypothesized link between thickness of cornea and stages of diabetic retinopathy.

The recent noncontact specular microscope to study corneal thickness and endothelium employ automated interfacing for finding picture through discrete focus technology.

Considering the larger diabetic population in India and paucity of literature especially in India, various few studies are proposed to evaluate central corneal thickness changes and corneal endothelial changes using specular microscopy in patient of diabetes mellitus with diabetic retinopathy and without diabetic retinopathy.

2. REVIEW OF LITREATURE

2.1 Diabetes Retinopathy and Duration of Diabetes

Diabetes is a chronic condition associated with variability of complications including diabetic retinopathy. Association between duration of DM and DR has been found in various studies across the globe. Mathur et.al demonstrated in their study that Mean period of diabetes at time of DR onset ranged from 6 years for people with type 2 diabetes to 15 years for people with type 1 diabetes with interval ∼5 years longer for onset of severe DR. Each 5-year rise in the period of diabetes at standard baseline was accompanying with a 17% increase in the risk of DR (95%CI 1.16 to 1.18) and a 42% intensification in the possibility of severe DR (95%CI 1.39 to 1.45) after modification for all other factors [5].

Gupta et al. [6] had originate that insulin in need of had more prevalence of DR (52.9% vs. 16.3%, P <0.0001) and sight vision threathening DR (19.1% vs. 2.4%, P <0.0001) in comparison to not on insulin but oral hypoglycaemic drugs. The incidence of diabetic retinopathy was considerably associated with longer duration (≥5 years).

In Tamil Nadu, Fredrick et al. [7] did a cross-sectional survey among patients with T2DM attending two primary health centres for treatment and follow-up. Among 270 patients were taken for 48 months. The prevalence of diabetic retinopathy was 29.6%. Overall, 65.9% of patients had hypertension, 14.4% had kidney releated disorder and 67.4% had diseases of peripheral nerves .Amongst patients with comorbid conditions 60%, 48%, 32%, and 3% were already diagnosed to have hypertension, neuropathy, retinopathy and kidney damage related to diabetes respectively. The risk factors for diabetic retinopathy were hypertension, extent of T2DM >5 years, reduced glycemic control, and nephropathy.

Patients with diabetes interval more than one decade had more corneal irregularities, predominantly in cell size that is coefficient of variation , compared with normal subjects. The central corneal thickness was significantly correlated with diabetes duration after controlling for age. The endothelial cell density and percentage of hexagonal cells were lower for diabetes >10 years' duration than for diabetes less than a decade '(p>0.05). CCT was correlated with duration of diabetes (p<0.05), but

endothelial cell loss was not found significant (p<0.05) [8].

3. IDENTIFICATION OF CORNEAL ABNORMALITY IN DIABETIC RETINOPATHY

There was challenge for identification and repetitively measuring of abnormal changes of the cornea. In past, corneal parameters study traditionally by observing central corneal thickness (CCT), corneal curvature (K), and transparency, all these were measure by use of various devices such as keratometers, autokeratometers, slit lamps, corneal topographies, corneal tomographies and confocal microscopes [9]. Corneal optical density was utilized for describing biological and histological features of cornea. Corneal optical density, as single biological and histological technique, was narrowly related with corneal transparency and might be utilize for describing degree of corneal transparency [10]. Endothelial cell analysis plays an essential part in routine clinical day to day practice of ophthalmologist as it provides valuable idea on corneal function and viability and further surgical related complications . Additionally, valuations of corneal thickness had been expected as substitute marker of endothelial barrier dysfunction among DM, due to direct physical effects of high blood glucose level and on corneal hydration [11].

Past study had shown that in area of inflammation, corneal optical density was higher comparing to remaining normal area, even when injuries were repaired (one month later). Hence, corneal optical density was utilized for examining inflammatory response and guiding futher evaluation of progress after corneal surgical procedure [10]. Pentacam was camera that was designed on basis of the Scheimpflug theory. It was capable of attaining three-dimensional images for evaluation of different parameters, along with cornea, crystalline lens, and atria [9,11,12]. It had been confirmed that Pentacam objectively evaluates nubecula through quantitative measurement of cornea density [13].

3.1 Various Studies for Effect Diabetes on Cornea

Previous research study accompanied in Vellor, India, among 153 patients with high blood glucose level and 163 age-matched controls, was done on patients before operative and after cataract surgical procedure up to 3 months postoperatively. They found no relevant difference in preoperative examinations between groups in any of central corneal thickness and corneal endothelial cell count. Both DM patients and control groups had reductions in endothelial counts and upsurge in morphological abnormalities (increase in cell sizes or polymegathism and increased variability of shape called pleomorphism) at 6 weeks and 3 months post-operation. They also found among control group the rate of count of corneal endothelial cells loss between 6 weeks to 3 months after cataract surgery was comparatively mild comparing to group of diabetes mellitus (p=0.023) [14]. However, the final evaluation measurements were non-significantly dissimilar at any time points, proposing that none of variances revealed were objectively relevant. It was observed that the Indian study assessed only small incision manual cataract surgical procedure however in but did not evaluated phacoemulsification cataract surgical procedure the latter was the more common form of surgery in the developed world and possibly prompts more corneal endothelial cell loss than manual small incision cataract surgery surgery [15].

A case control study conducted by Ozdamar et al. [16] for evaluation of relationship of central corneal thickness with 245 DM patients and compared it with age and sex-matched 145 controls. They had subdivided DM patients into 3 subsections: subdivision 1 (no diabetic retinopathy), subdivision 2 (non-proliferative diabetic retinopathy), and subdivision 3 (proliferative diabetic retinopathy).They found that socio-demographic data characteristics of study and controller groups were almost analogous (p>0.05). The mean central corneal thickness was significantly higher among DM patients as compared to control group (564±30μm vs 538±35μm; p=0.001). Moreover, mean CCT was found to be higher in subgroup 3 (582±23μm) comparing with subdivision 1 (565±32μm) and subdivision 2 (558±31 μm); but the difference did not reach statistical significance (p=0.056). In addition, there was no substantial association in reverence to level of HbA1c and illness interval among subgroups.

A study by Lee et al. [17] had found that diabetes patients had thick cornea (588.2±2.7 μm) compared to controls (567.8± 3.8 μm; p<0.05). Additionally, they found that thickness of corneal was significantly high among diabetes with duration of >10 years comparing to <10 years diabetes duration (p<0.05). Similarly, duration of

diabetes in Parekh et al. [18] study had significant association with increase in thickness of cornea cell ($p<0.05$) and further they identified significant increase in cornea thickness with increase in diabetes severity ($p<0.05$). A case-control study by Chauhan et al. [19] had found mean values of CCT among DM patients (520.1±25.4 µm) was significantly higher than mean CCT values of control groups (515 ± 21.8 µm; $p<0.05$).

Conversely, a study by El-Agamy and Alsubaie [20] had found non-significantly higher level of CCT among non-DR patients compared to DR patients and controls ($p>0.05$). In Chowdhari et al. [21] study, they found non-significantly higher level of CCT among non-DR patients compared to DR patients and controls ($p>0.05$). A study by Toygar et al. [22] had found that average CCT was significantly higher among diabetic patients (non-DR, NPDR and PDR groups) compared to compared group ($p<0.05$). Though CCT values among non-DR patients did not significantly vary from DR patients ($P = 0.64$). Likewise, there were non-significance variance in corneal thickness values between Non PDR and proliferative diabetic retinopathy patients ($p>0.05$). Moreover, they found that CCT was significantly correlated with IOP and average IOP values of diabetic were non-significantly higher compared to controls.

A population based case-control study was conducted by Sudhir et al. [23] for studying corneal endothelial cell density and morphological features among T2DM patients (cases) and compared them with nondiabetics (controls). They selected 1191 T2DM cases and 121 controls. The mean corneal endothelial cell density was lower among T2DM patients comparing to controls (2550±326 vs 2634±256 cells/mm^2; $p=0.001$). There was non-significant variance found in hexagonality, mean values on pachymetry and coefficient of variation among T2DM patients and controls. After adjusting for age, multivariate regression analysis had shown mean cell density to be smaller by 66 cells/mm^2 (95%CI 6.3-125.9) among T2DM patients compared with nondiabetic controls.

Chowdhari et al. [21] had found that among DR patients 70.2% had NPDR and 29.8% had PDR. There was statistically non-significant relationship of CCT, endothelial CD, CV and hexagonality with severity of diabetic retinopathy ($p>0.05$). In Ozdamar et al. [4] study, there was non-significantly higher mean vales of CCT in PDR patients (582±23µm) compared to non-DR (565±32µm) and NPDR (558±31 µm; $p>0.05$).

A prospective cross-sectional study was conducted by Irfan Durukan [23] for evaluation of morphological features of corneal endothelial cells and their relationship with stage of retinopathy among 120 DM patients and compared them with 112 control groups. Depending on fundus findings, DR were divided into no-DR, non-proliferative DR and proliferative DR. They found that hexagonal cell rate and endothelial cell density were lower among DM group, while central corneal thickness was higher among DM group compared to controls. However, average cell area and co-efficient variation of cell area had non-significant differences between DM and control groups. Among subgroups of DM patients, there was significant difference for endothelial cell density and diminished as there is advanced diabetic retinopathy raises. The mean cell area, co-efficient variant of cell area and central thickness of corneal dimensions were almost same among DM subgroups. Hexagonality values were significantly contradictory between subgroups, with lower ratio of hexagonal cells among proliferative DR group.

A comparative study done by Tasli et al. [24] for determining association of corneal morphological features with general characteristics and investigation done in laboratory of DM patients, along with DM period. They included 195 DM patients and 100 controls in study. They found that Endothelial cell density (ECD) and hexagonal cell ratio were significantly lower, while average cell size, coefficient of variation in size of endothelial cell (CV%), and central corneal thickness (CCT) were considerably greater among DM patients compared to controls ($p=0.001$).Among diabetic retinopathy patients, ECD and hexagonal cell ratio decreased, while average cell size, CV%, and CCT augmented. Furthermore, correlation analysis of corneal morphological features and laboratory data of DM patients, had shown significant negative correlation of ECD with diabetes duration ($p=0.028$). HbA1c levels, urinary albumin-creatinine ratio ($p=0.041$), average cell size and CV% had shown positive correlation with these parameters.

Two previous studies conducted on corneal morphology had found that DM to be related with greater corneal thickness [25,26], which was reliable with findings former than 2008. It was

notable that patients with proliferative, non-proliferative diabetic retinopathies and those with no diabetic retinopathies did not have significantly different corneal thickness [26–27]. Furthermore, a study in Romania among hundred children between mean age of 6–17 years with type 1 DM had found higher thickness of central cornea comparing with an comparable number of children of similar age [28], and same evaluation was been reported in Turkey also [25].

A study by Ozdamar et al. [4] had found that mean CCT was significantly higher among DM patients as compared to control group ($p<0.01$). In Tasli et al. [29] study, they had found that CCT were significantly higher among DR patients compared to non-DR and controls ($p<0.05$). In Ramakrishnan et al. [30] study, there was significantly higher mean corneal thickness in diabetic group compared to control group ($p<0.05$). A study done by Irfan Durukan [31] had found that CCT was higher among DM group compared to controls.

Conversely, a study by El-Agamy and Alsubaie [20] had found non-significantly higher level of CCT among non-DR patients compared to DR patients and controls ($p>0.05$). In Chowdhari et al. [21] study, they found non-significantly higher level of CCT among non-DR patients compared to DR patients and controls ($p>0.05$). A study by Toygar et al. [22] had found that average CCT was significantly higher among diabetic patients (non-DR, NPDR and PDR groups) compared to control group ($p<0.05$). Though CCT values among non-DR patients did not significantly vary from DR patients ($P = 0.64$). Likewise, there was non-significant variance in measurement of corneal central thickness between Non proliferative and Proliferative changes in diabetic patients ($p>0.05$). Moreover, they found that CCT was significantly correlated with IOP and average IOP values of diabetic were non-significantly higher compared to controls.

A cross-sectional study conducted by Yoo and Tae [32] for evaluation of differences in corneal endothelial cell morphology and corneal thickness in T2DM patients and related them for age, disease duration, and HbA1c to non-diabetic patients. They included 511 T2DM patients (1022 eyes) and 900 non-diabetic patients (1799 eyes). They found that among all age groups, the subjects with T2DM had shown significantly lower endothelial cell density (ECD), hexagonality, higher CV, and thicker CCT compared to non-diabetic. This difference was more noticeable among long duration DM (more than ten years) patients & higher HbA1c (more than equal to seven percent) [33,34]. When stratified by age criteria, from 60 years groups, corneal endothelial cell findings had shown significantly alteration among DM and controls.

4. CONCLUSION AND RECOMMENDA-TIONS

- With advancement in technologies, better availability of hospital infrastructure every diabetic patients shall be screened for identifying early changes of Cornea
- Further studies are required with larger sample size in different geographical area for making generalized findings.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFRENCES

1. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract. 2014;103(2):137–49.
2. Agroiya P, Philip R, Saran S, Gutch M, Tyagi R, Gupta KK. Association of serum lipids with diabetic retinopathy in type 2 diabetes. Indian J Endocrinol Metab. 2013;17(Suppl1):S335.
3. Das A, McGuire PG, Rangasamy S. Diabetic macular edema: Pathophysiology and novel therapeutic targets. Ophthalmology. 2015 Jul;122(7):1375–94.
4. Ljubimov A V. Diabetic complications in the cornea. Vision Res. 2017;139:138–52.
5. Mathur R, Bhaskaran K, Edwards E, Lee H, Chaturvedi N, Smeeth L, et al. Population trends in the 10-year incidence and prevalence of diabetic retinopathy in the UK: a cohort study in the Clinical

Practice Research Datalink 2004–2014. BMJ Open. 2017 Feb;7(2):e014444.

6. Gupta A, Delhiwala KS, Raman RP, Sharma T, Srinivasan S, Kulothungan V. Failure to initiate early insulin therapy–A risk factor for diabetic retinopathy in insulin users with Type 2 diabetes mellitus: sankara Nethralaya-Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN-DREAMS, Report number 35). Indian Journal of Ophthalmology. 2016 Jun;64(6):440.
7. Sunita M, Singh AK, Rogye A, Sonawane M, Gaonkar R, Srinivasan R, et al. Prevalence of diabetic retinopathy in urban slums: The aditya jyot diabetic retinopathy in urban Mumbai Slums Study-Report 2. Ophthalmic Epidemiol. 2017 Apr;1–8.
8. Lee JS, Oum BS, Choi HY, Lee JE, Cho BM. Differences in corneal thickness and corneal endothelium related to duration in diabetes. Eye. 2006;20(3):315–8.
9. Lanza M, Cennamo M, Iaccarino S, Romano V, Bifani M, Irregolare C, et al. Evaluation of corneal deformation analyzed with a Scheimpflug based device. Contact Lens Anterior Eye. 2015;38(2):89–93.
10. Cennamo G, Forte R, Aufiero B, La Rana A. Computerized Scheimpflug densitometry as a measure of corneal optical density after excimer laser refractive surgery in myopic eyes. J Cataract Refract Surg. 2011;37(8):1502–6.
11. Beato JN, Esteves-Leandro J, Reis D, Falcão M, Rosas V, Carneiro Â, et al. Evaluation of corneal structure and endothelial morphological characteristics in type 2 diabetic and non-diabetic patients. Clin Ophthalmol (Auckland, NZ). 2020;14:1993.
12. Rosales P, Marcos S. Pentacam scheimpflug quantative imaging of the crystalline lens and intraocular lens. 2008;69.
13. Kolb H, Mandrup-Poulsen T. The global diabetes epidemic as a consequence of lifestyle-induced low-grade inflammation. Diabetologia. 2010;53(1):10–20.
14. Takacs AI, Mihaltz K, Nagy ZZ. Corneal density with the Pentacam after photorefractive keratectomy. J Refract Surg. 2011;27(4):269–77.
15. Mathew PT, David S, Thomas N. Endothelial cell loss and central corneal thickness in patients with and without diabetes after manual small incision cataract surgery. Cornea. 2011;30(4):424–8.
16. Dhasmana R, Singh IP, Nagpal RC. Corneal changes in diabetic patients after manual small incision cataract surgery. J Clin diagnostic Res JCDR. 2014;8(4):VC03.
17. Ozdamar Y, Cankaya B, Ozalp S, Acaroglu G, Karakaya J, Özkan SS. Is there a correlation between diabetes mellitus and central corneal thickness? J Glaucoma. 2010;19(9):613–6.
18. Shih KC, Lam KS-L, Tong L. A systematic review on the impact of diabetes mellitus on the ocular surface. Nutr Diabetes [Internet]. 2017;7(3):e251–e251. Available:https://doi.org/10.1038/nutd.2017.4
19. Browning DJ, Glassman AR, Aiello LP, Beck RW, Brown DM, Fong DS. Diabetic retinopathy clinical research network relationship between optical coherence tomography-measured central retinal thickness and visual acuity in diabetic macular edema. Ophthalmology. 2007;114(3):525–36.
20. Vieira-Potter VJ, Karamichos D, Lee DJ. Ocular complications of diabetes and therapeutic approaches. Biomed Res Int. 2016;2016.
21. Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of diabetic retinopathy in urban India: The Chennai Urban Rural Epidemiology Study (CURES) eye study, I. Invest Ophthalmol Vis Sci. 2005;46(7):2328–33.
22. Sanchis-Gimeno JA, Alonso L, Rahhal M, Bastir M, Perez-Bermejo M, Belda-Salmeron L. Corneal thickness differences between type 2 diabetes and non-diabetes subjects during preoperative laser surgery examination. J Diabetes Complications. 2017 Jan;31(1):209–12.
23. Gadkari SS, Maskati QB, Nayak BK. Prevalence of diabetic retinopathy in India: The all India ophthalmological society diabetic retinopathy eye screening study 2014. Indian J Ophthalmol. 2016;64(1):38–44.
24. 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 Oct;31(10):1119–22.

25. Durukan I. Corneal endothelial changes in type 2 diabetes mellitus relative to diabetic retinopathy. Clin Exp Optom. 2020 Jul;103(4):474–8.
26. Taşlı NG, Icel E, Karakurt Y, Ucak T, Ugurlu A, Yilmaz H, et al. The findings of corneal specular microscopy in patients with type-2 diabetes mellitus. BMC Ophthalmol [Internet]. 2020 Jun 3;20(1):214. Available:https://pubmed.ncbi.nlm.nih.gov/32493325
27. Akinci A, Bulus D, Aycan Z, Oner O. Central corneal thickness in children with diabetes. J Refract Surg. 2009;25(11):1041.
28. Toygar O, Sizmaz S, Pelit A, Toygar B, Kiziloğlu ÖY, Akova Y. Central corneal thickness in type II diabetes mellitus: is it relatedto the severity of diabetic retinopathy? Turkish J Med Sci. 2015;45(3):651–4.
29. Nishitsuka K, Kawasaki R, Kanno M, Tanabe Y, Saito K, Honma K, et al. Determinants and risk factors for central corneal thickness in Japanese persons: The Funagata Study. Ophthalmic Epidemiol. 2011;18(5):244–9.
30. Tiutiuca C. Assessment of central corneal thickness in children with diabetus mellitus type I. Oftalmol (Bucharest, Rom. 1990;2013;57(1):26–32.
31. Zheng Y, He M, Congdon N. The worldwide epidemic of diabetic retinopathy. Indian J Ophthalmol. 2012 Jun;60(5):428–31.
32. de Barros Garcia JMB, Isaac DLC, Avila M. Diabetic retinopathy and OCT angiography: Clinical findings and future perspectives. Int J Retin Vitr. 2017 Mar;3:14.
33. Ye H, Lu Y. Corneal bullous epithelial detachment in diabetic cataract surgery. Optom Vis Sci. 2015;92(7):e161–4.
34. Kim YJ, Kim TG. The effects of type 2 diabetes mellitus on the corneal endothelium and central corneal thickness. Sci Rep [Internet]. 2021 Apr 15;11(1):8324. Available:https://pubmed.ncbi.nlm.nih.gov/33859349

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