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Research Article

Central Corneal Thickness Changes in Diabetic Retinopathy. A Prospective Observational and Correlative Study

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Abstract: Generally, there is a delay of 4 to 7 years in the diagnosis of type 2 diabetes and about 20% of patients would have already developed some micro vascular complications at the time of diagnosis. To study the central corneal thickness (CCT) variation and correlate with grades of diabetic retinopathy in an adult South Indian population. The study was conducted on 184 eyes each of T2DM patients of duration more than 5 years. 98 males (53.26%) & 86 females (46.73%) were recruited. After recording age, sex and duration of diabetes, fundus examination was done. CCT measurements were determined using Ultrasonic Pachymetry. Diabetic retinopathy was classified based on ETDRS (Early diabetic retinopathy study) and mean CCT values of each group were correlated and statistically analysed using SPSS software Version 17. Out of 184 subjects recruited, 72 patients were with no diabetic retinopathy (NDR), 107 patients were with non-proliferative diabetic retinopathy (NPDR) and 5 patients were with proliferative diabetic retinopathy (PDR). The mean CCT of no diabetic retinopathy (NDR), non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) were found to be 526.14µm, 533.98µm and 555.20µm respectively. CCT was found to be thicker for diabetics with proliferative diabetic retinopathy compared to those with no retinopathy; the difference was not statistically significant (p=0.16). Uncontrolled diabetics (HbA1c >7%) had thicker corneas compared with diabetics with good control which was statistically significant (p=0.003). CCT was higher in diabetics having duration > 10 years than with duration <10 years but was not statistically significant (p=0.117).

Key Words: Type 2 Diabetes Mellitus, Grades of Diabetic Retinopathy, Central Corneal Thickness, HbA1c and Ultrasound Pachymetry.

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1. INTRODUCTION

Diabetes Mellitus is a global health problem. In the 21st century, it is considered to be one of the most common of the metabolic diseases.[1] It affects about 415 million adults and by 2040 the figure will reach 640 million.[2] Vascular and non-vascular complications associated with this disease are the most important causes of morbidity and mortality in such patients. Generally, there is a delay of 4 to 7 years in the diagnosis of type 2 diabetes and about 20% of patients would have already developed some micro vascular complications at the time of diagnosis[3]. Central corneal thickness is an important indicator of corneal health and integrity. CCT measurement by ultrasound pachymetry has been used as diagnostic modalities in ectatic corneal dystrophies which include keratoconus, pellucid marginal degeneration, dry eye and contact lens related problems.[4] 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.[5]In 70% of diabetic population, diabetic keratopathy is seen due to polymegathism, pleomorphism, decrease corneal hexagonality, decreased endothelial cell density, low corneal sensitivity and increased CCT.[6]Earliest clinically detectable change in cornea in diabetics is increased corneal thickness.[4]Significantly higher CCT values in diabetic population as compared to healthy age matched controls had been reported by various authors[7, 8-10]Previous population-based and hospital-based investigations, such as Rotterdam Study, Mongolian study, Reykjavik Eye Study, Barbados Eye Study, Tajimi study, and Singapore Malay Eye Study, have assessed CCT in various population, which includes Caucasians, Hispanics, Mongolians, Japanese, Chinese etc.[11-14]However, studies focused on CCT have been very few in India.[15,16] Very few studies are done based on CCT in relation to duration of diabetes, severity of diabetic retinopathy and on glycemic control.Diabetes mellitus is a serious and expanding health problem worldwide as a result of unhealthy and sedantary lifestyles along with population aging. Diabetes has been linked to primary open-angle glaucoma in several studies. People who had diabetes had thicker corneas, according to limited evidence from population-based research. In this regard, central corneal thickness (CCT) has been linked to the development and worsening of glaucoma. The aim of our study was to compare central corneal thickness in type 2 diabetes mellitus (DM) patients of more than 5 years duration with severity of diabetic retinopathy in South Indian population and to analyze the correlation of CCT in relation to duration and severity of diabetes and with level of glycosylated hemoglobin (HbA1c) / the glycaemic status.

2. MATERIALS AND METHODS

It was a prospective clinical study done at a tertiary care center, between Jan 2019 to Feb 2020. The study was conducted 184 selected diabetes patients.

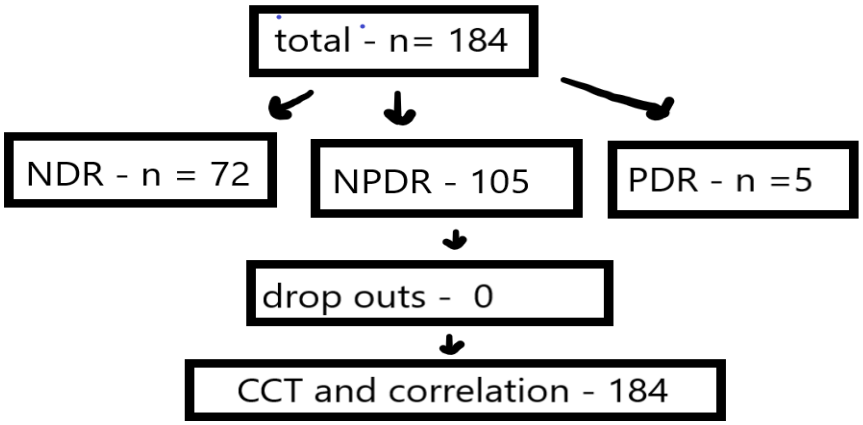
2.1 Inclusion and exclusion criteria

The inclusion criteria includes patients with Type 2 diabetes mellitus (T2DM) of duration more than 5 years. Right eye of every individual was studied and left eye was taken up in case of any disease in right eye that prevents visualization of fundus. The exclusion criteria: Individuals with history of ocular infection, inflammation, trauma, surgery or photocoagulation were excluded from the study. Diagnosed cases of glaucoma and individuals on any eye drops or using contact lenses were excluded. A total sample size of 184 patients were included in the study.

2.2 Study protocol

Informed consent from each patient was taken and age, sex, duration of diabetes and latest HbA1c level were recorded. After recording visual acuity and detailed examination on slit lamp patient was subjected to IOP measurement and fundus examination. 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 (NDR), Group 2 with non-proliferative diabetic retinopathy (NPDR), Group 3 with proliferative diabetic retinopathy (PDR).

2.3 Consort flow chart



The CCT measurement was done in seated patient using a contact ultrasonic pachymeter [DGH 555B (USA) -Pachette 4] probe gently placed in the mid-pupillary axis of the cornea in undilated eye after instillation of 0.5% topical proparacaine.

3. STATISTICAL ANALYSIS

The mean of three readings were taken. Mean CCT values were then correlated with severity of diabetic retinopathy and was statistically analysed using SPSS software version 17. Considering 5 % of a 500 population visiting the hospital, a sample size of 64 is enough for a power of 90 with 95 % confidence interval

In this cross-sectional comparative study, the study population included 184 subjects with type 2 diabetic mellitus (T2DM) of duration more than 5 years. The study group was divided into 3 groups, according to ETDRS classification as 'no diabetic retinopathy (NDR) in group 1 [n=72], Non-proliferative diabetic retinopathy in group 2 [n=107] and proliferative diabetic retinopathy in group 3 [n=5]', depending on the severity of diabetic retinopathy. (Fig.1)

4. RESULTS

TABLE 1 : Correlation of CCT with duration of diabetes in each group.

Duration Of diabetes	GROUP 1 (NDR) N=72	GROUP 2 (NPDR) N=107	GROUP 3 (PDR) N=5	Mean CCT (µm)	P Value
5- 10 years	64 (88.9%)	82 (76.6%)	4 (80%)	522.97 ± 8.66	0.117
> 10 years	8 (11.1%)	25 (23.4%)	1 (20%)	534.51 ± 8.12	

CCT was found to be higher in patients with longer duration of DM but the difference was not statistically significant (p= 0.117). Duration of diabetes between groups were correlated using Anova test and it was also not found statistically significant. (p=0.097). [Table.1]

TABLE 2 : Variation of CCT (µm) with HbA1c (mg/dl) level in each groups.

	Mean CCT in GROUP 1 (NDR) N=72	Mean CCT in GROUP 2 (NPDR) N=107	Mean CCT in GROUP 3 (PDR) N=5	Overall CCT (GROUP 1, 2 and 3) N=184
HbA1c <7%	524.19 ± 9.07	528.80 ± 13.45	0	526.14 ± 11.95
HbA1c ≥7%	526.94 ± 12.94	534.65 ± 56.11	555.00 ± 4.95	555.98 ± 49.49
P Value	0.11	0.64	-	0.003

Mean CCT values increased in patients with poor control of diabetes. Using T-test, there was no significant change in CCT among NDR, NPDR and PDR groups. But overall CCT change between them with HbA1c <7% and ≥7% was found to be statistically significant. (p=0.003). [Table. 2]

TABLE 3 : Variation of CCT (µm) with severity of retinopathy.

	Number of patients(N)	Mean CCT (µm)	P Value
Group A (NDR)	72	526.14 ± 11.95	0.162
Group B (NPDR)	107	533.98 ± 49.49	
Group C (PDR)	5	555.20 ± 4.95	

The mean CCT values increased with severity of diabetic retinopathy from no diabetic retinopathy (NDR) to proliferative diabetic retinopathy (PDR). But increased central corneal thickness using Anova test did not show any statistical significance. (p=0.162). [Table.3]

According to Pearson correlation analysis, CCT did not show any significant difference with duration and severity of diabetes mellitus but was found to have significant correlation with levels of glycosylated hemoglobin (HbA1c).

5. DISCUSSION

Our study showed that central corneal thickness progressively increased with the severity of diabetic retinopathy but the variation was not statistically significant. However, studies done by Roszkowska et al, Lee et all, Beata Urban et al and Stella Briggs supported our study with the fact that increased CCT is seen in diabetics.[17-20] This is explained by the fact that increased CCT is due to greater pleomorphism and polymegathism in their corneas as concluded by another study. But Mc Namara et al, Weston et al and Su et al suggested that the endothelial structure is altered in hyperglycemia leading to corneal hydration which increases corneal thickness.[21-24] The findings of our study were found to be correlating with studies done by ozdamer et al and choo et al which shows that diabetics with proliferative retinopathy was found to have thicker central corneal thickness than those with non-proliferative diabetic retinopathy and no diabetic retinopathy but the difference was not statistically significant.[25,26] More recent studies by Toygar et al and Mathebula et al stated that increased CCT in diabetes irrespective of severity of retinopathy.[27,28] Diabetic patients in our study with duration of >10 years had significantly thicker corneas as compared to diabetics with duration of <10 years but the difference was not statistically significant. This observation was reinforced in a study done by Lee et al, Beata Urban et al.[18,19] This finding was

consistent also with the previous studies done by Siribunkum J et al.[29] However, few studies such as Ozdamar Y et al and Stella Briggs et al rejected its correlation with duration of diabetes.[15,20] Increased CCT in diabetics is explained by increased endothelial permeability and increased stromal swelling pressure because of accumulation of sorbitol or glycosylation of corneal collagen.[13] All these mechanism are seen in cases with poor glycemic control and longer duration of diabetes. It was noted in our study that there was a significant positive correlation between HbA1c and CCT which was supported by studies done by Su et al and Wiemer et al .[24,] While few studies by Beata et al, Ozdamer et al and Choo et al have reported no correlation .[19,25,26]This could possibly be explained by the fact that structural and functional changes are seen in corneal endothelium in patients with uncontrolled diabetes.[8,3,13] Limitations of this study were that it was a single point study with small sample size and confounding factors like smoking and other co-morbidities were not taken into account. Results of this study shall provide a greater insight into the understanding of corneal morphology in diabetics especially in the context of pre-operative evaluation and glaucoma diagnosis.

6. CONCLUSION

Central corneal thickness of diabetic patients increased with the severity of retinopathy but was not statistically significant. Mean CCT values were significantly correlated with HbA1C levels. Duration of diabetes did not have any influence on central corneal thickness.

7. AUTHOR CONTRIBUTION

Avuno Keditso – data collection – **and** Srikanth. K – design and write up.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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