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STUDY OF CENTRAL CORNEAL THICKNESS (CCT) IN DIABETICS IN EUGLYCEMIC STATE AND HYPERGLYCEMIC STATE.

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ABSTRACT
Diabetes Mellitus is characterized by chronic hyperglycemia, leading to systemic complications affecting various organs, including the cornea. This prospective longitudinal observational study aimed to investigate changes in Central Corneal Thickness (CCT) among Type 2 diabetics in hyperglycemic and euglycemic states over a one-month period. A total of 90 diabetic subjects were enrolled, with CCT within 30 mins of post-prandial blood sugar (PPBS) measurements. Follow-up assessments were conducted after one month to evaluate CCT changes under euglycemic conditions, defined as PPBS < 200 mg/dl with at least 50 mg/dl reduction from hyperglycemic levels.
Results: indicated no significant difference in CCT between hyperglycemic and euglycemic states ($p > 0.05$). Furthermore, there was no correlation found between changes in blood sugar levels and CCT alterations. Short-term fluctuations in blood sugars did not influence CCT in diabetic patients within the study period. Additionally, routine Intraocular Pressure (IOP) measurements were unaffected by short-term variations in blood sugar levels.
In conclusion, this study suggests that short-term glycemic fluctuations may not impact corneal thickness or routine IOP measurements in Type 2 diabetes, highlighting the stable nature of these ocular parameters despite glycemic variability over one month.

KEYWORDS: Central corneal thickness, Diabetics, Euglycemia, Hyperglycemia, Intraocular pressure.

INTRODUCTION

Diabetes Mellitus is a set of metabolic disorders or syndromes where there is hyperglycemia due to abnormalities in insulin secretion or activity.[1]. In diabetics, chronic hyperglycemia is linked to long-term damage, malfunction, and failure of several organs, including the kidneys, blood vessels, nerves, and eyes.[2].
The morphology, physiology, and clinical appearance of the cornea are all negatively impacted by diabetes mellitus [3]. These alterations appear in nearly every layer of the cornea, including the stroma, endothelium, corneal epithelium, and epithelial basement membrane complexes.[4]
Advanced glycosylation end products (AGEs) can be produced by elevated protein glycosylation brought on by hyperglycemia linked to diabetes.[4] Research has indicated elevated AGE levels in the corneas of elderly diabetics. Increased collagen cross-linking brought on by elevated AGEs in tissues causes the cornea's structure to gradually harden, altering its biomechanical characteristics.[5] Its role in alterations of corneal thickness hasn't been investigated independently, though.
Rather than abrupt fluctuations in blood sugar levels, the effects of chronic hyperglycemia are probably responsible for the structural and functional alterations observed in diabetics.[6] Short-term alterations in CCT in hyperglycemic states have not been investigated in diabetics, despite changes in refraction and lens thickness being reported in these conditions.Therefore, we wanted to gather information to see whether diabetics' CCT changed when their blood sugar levels were high (hyperglycemic condition) and when they were remeasured when their blood sugar levels were under control (euglycemic state).

MATERIALS AND METHODS

This is a Prospective longitudinal observational study conducted at Saveetha Medical College and Hospital from August 2023 to June 2024 after taking approval from ethics committee.Subjects were chosen from General medicine outpatient department and ophthalmology outpatient department with T2DM in Hyperglycemic state. The study included patients who met the inclusion criteria.

Hyperglycemic state was defined as – PPBS ≥ 200 mg/dl and

Euglycemic state was defined as – PPBS < 200 mg/dl along with minimum 50 mg/dl reduction of PPBS as compared to their hyperglycemic state.

Criteria for Inclusion

1. Diabetic patients in hyperglycemic state
2. Patients of either sex
3. Patients who agree to follow up
4. Patients who are in the age group of 18-80

Criteria for Exclusion

1. Individuals who have already had eye surgery
2. Those who wore soft contact lenses seven days before their ophthalmic evaluation and hard contact lenses for the month before
3. People with any kind of corneal disease, including corneal edema, degenerations, keratoconus, illnesses involving collagen, glaucoma, intraocular inflammation, and ocular surface abnormalities
4. Uveitis sufferers
5. Patients who object to the research or follow-up
6. Patients under the age of eighteen

METHODOLOGY

The lead investigator of the trial examined all diabetic patients receiving blood sugar readings whose post-PPBS levels were > 200 mg/dl (hyperglycemic state). If they met the inclusion and exclusion criteria after giving their informed consent, they were recruited in the study. The CCT measurement was completed 30 minutes after the blood sugar check.

An optical biometer called the Nidek AL scan (Nidek Co, Ltd, Gamagori, Japan) was used to measure CCT.

In accordance with the standard management procedure, these patients were contacted for follow-up assessments one month later, after which any adjustments to the anti-diabetic drugs that the treating physician recommended were made

Those patients who achieved euglycemia had their CCT values collected for analysis. CCT measures were repeated at the next month's follow-up if the patients did not meet the aforementioned requirements during the one-month visit. If the patients met the necessary criteria during the study period, the measurements were included in the analysis. The patient's right eye readings were taken into the study. The left eye was taken for analysis if the right eye did not meet the inclusion and exclusion requirements but the left eye did.

RESULTS

Between August 2023 and June 2024, 120 diabetic individuals (120 eyes) in total were assessed. Of these, 96 eyes reached euglycemia at one month, as specified in the plan of action. At one month, eight patients were lost to follow-up, and the remaining patients did not reach euglycemia. Of those who did not reach euglycemia at one month, a small number (6 patients) did so at three months; the remaining 10 patients either did not reach euglycemia during the research period or failed to follow up.

Table 1 .Baseline characteristics of the study patients

Total number of patients who achieved euglycemia	96
Number of males	27
Number of females	69
Average age(years)	52.39
Range of age(years)	26-75
average duration of diabetes(years)	7.2

Table 2 : Number of patients showing increased, decreased or no change in in CCT in euglycemic and hyperglycemic states

Total number of patients	96
No. of patients showing increase in CCT on achieving euglycemic state	40
No. of patients showing decrease in CCT on achieving euglycemic state	42
No.of patients showing no change in CCT on achieving euglycemic state	14

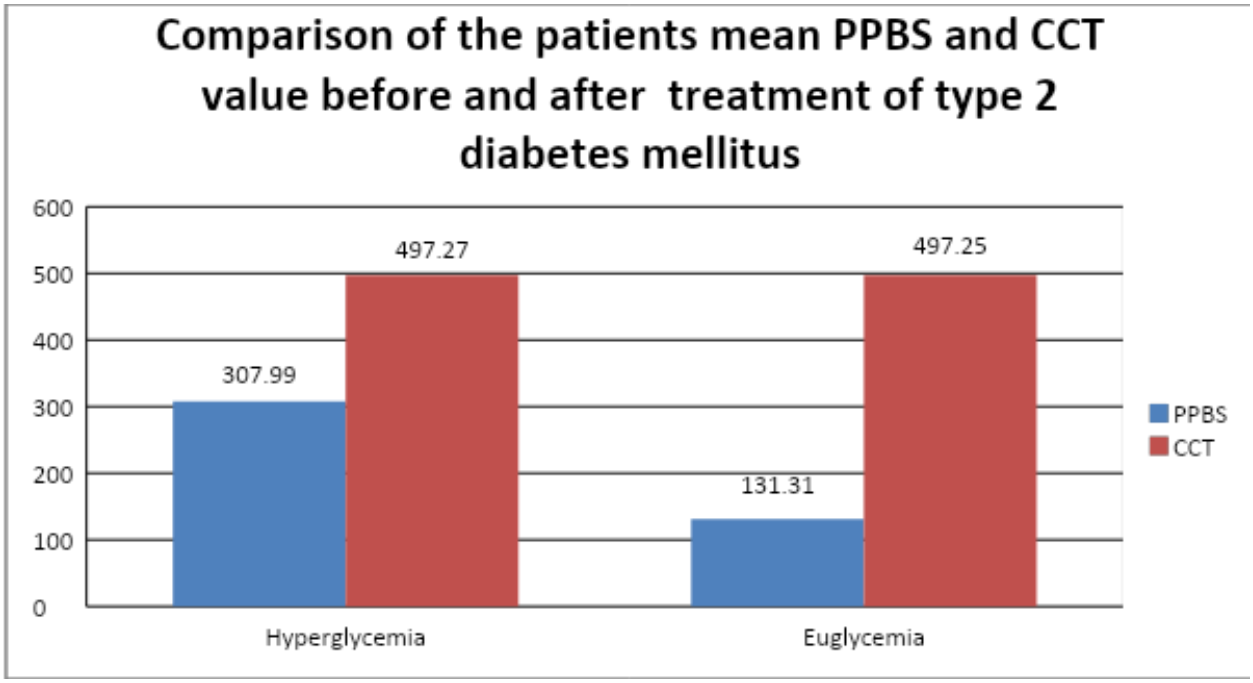
SPSS software (SPSS 16.0 for Windows, IBM Co.) was used to conduct the statistics. The Kolmogorov-Smirnov test was used to determine if the data had a normal distribution. Levene's test was used to establish the homogeneity of the variables. A student paired t test was used to compare variables with equal variance and a normal distribution before and after therapy. One-Way ANOVA test was compared between groups (reduction of blood sugar level and central corneal Thickness difference) and expressed their mean, standard deviation and its significance. Student T test was done to compare the mean,
standard deviation and significance of PPBS and CCT between male and female patients. Correlations between PPBS and CCT were done with Pearson’s correlation analysis before and after treatment. A p value lower than .05 - .01 was considered as statistically significant.

Table 3 Comparison of the patients mean PPBS and CCT value before and after treatment of type 2 diabetes mellitus.

Parameter	Blood glucose levels in Hyperglycemic state (At the beginning of the study) Mean +/- SD (96)	Blood glucose levels after achieving euglycemic state Mean +/- SD (96)	Mean Difference	SD Difference	T value	Sig
PPBS	307.99 +/- 60.68	131.31+/- 24.723	176.677	64.687	26.761	.000***
CCT	497.27 +/- 34.208	497.25 +/- 35.004	.021	4.670	.044	.965(NS)

There was a significant difference (decreases) in the mean blood glucose level (PPBS) at the beginning of the study (Hyperglycemia) (M= 307.99, SD= 60.68) and after one month of the successful treatment the mean blood glucose (euglycemia) (M=131.31, SD= 24.723), t(96)=26.761, p=.000*

There was not a significant difference in the CCT in Hyperglycaemia (M= 497.27, SD= 34.208) and in euglycemia (M=497.25, SD= 35.004), t (95) = .044, p=.965



PPBS –postprandial blood glucose level, CCT-Central corneal Thickness.

Fig 1 – Graph showing the mean difference of PPBS and CCT value before and after treatment of type 2 diabetes mellitus.

This graph showed that the PPBS mean value was higher at the beginning of the study and it decreased after the treatment of one month with anti diabetic drugs. This showed the statistical significance at the p value.000*. Regarding the central corneal thickness this graph showed that the mean value was almost equal at the beginning of the study

and also after the treatment of one month**.** So there was no statistical significance in the Central corneal Thickness during hyperglycemia and euglycemia.

Table 4: Correlation between CCT difference and PPBS difference correlations

		PPBS- diff (mg/dl)	CCT- diff (microns)
PPBS- diff (mg/dl)	Pearson Correlation (r)	1	.014
	Sig. (2-tailed)		.891
	N	96	96
CCT- diff (microns)	Pearson Correlation (r)	.014	1
	Sig. (2-tailed)	.891	
	N	96	96

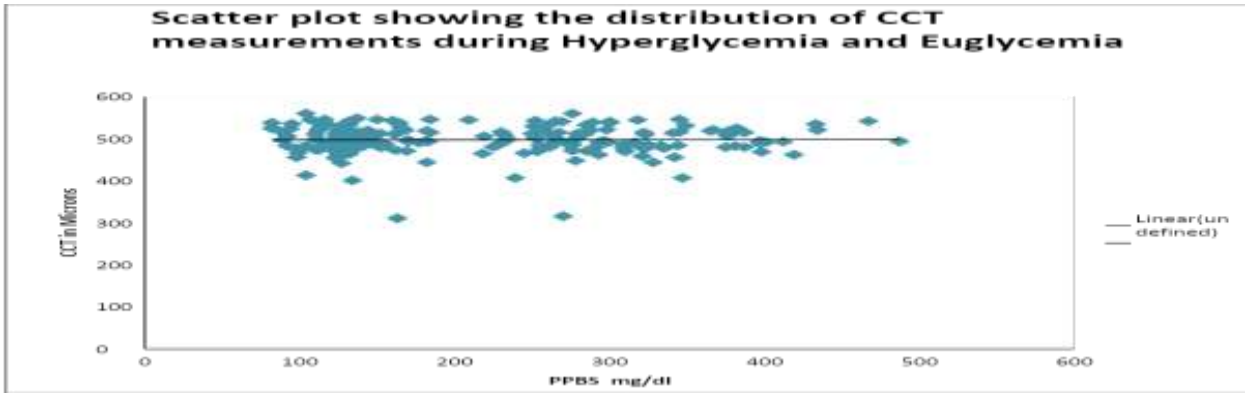
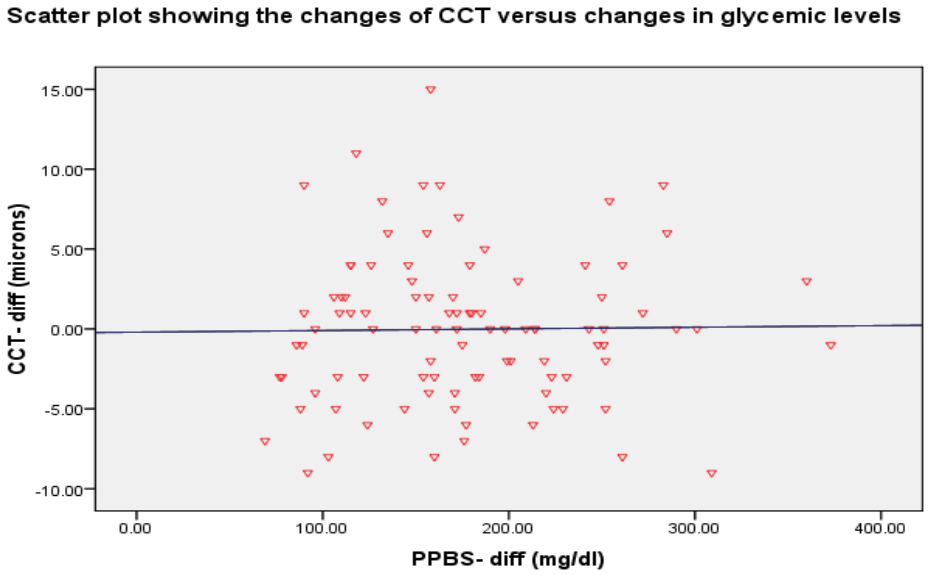


Fig-2: Scatter plot graph

This scatter plot showed that there was no correlation of distribution of CCT measurements during Hyperglycemia and Euglycemia (Pearson's r=.005)



R=.014

PPBS – diff, difference in PPBS between hyperglycemia and euglycemia, CCT- diff, difference in Central corneal Thickness during hyperglycemia and euglycemia.

Fig-3: Scatter plot graph

This scatter plot showed that there was no correlation between difference in PPBS and CCT during Hyperglycemia and Euglycemia (Pearson's r=.014)

Table 5 : CCT changes with the amount of blood sugar level reduction

Amount of reduction in Blood sugar	No. of sample	CCT (Microns) in Hyperglycemia Mean ± SD (Range)	CCT (Microns) in Euglycemia Mean ± SD (Range)	F Value	Sig**
Group -1 (50-100)	11	503.4 ± 30.15 (448 – 595)	501.3 ± 31.30 (444 – 542)	.273	.762(NS)
Group-2 (101-200)	54	497.2 ± 37.69 (316 – 560)	498.5 ± 38.21 (311 – 560)	.226	.798 (NS)
Group – 3 (201-380)	31	494.5 ±29.49 (407 – 542)	494.6 ± 30.90 (401 – 545)	1.96	.146 (NS)

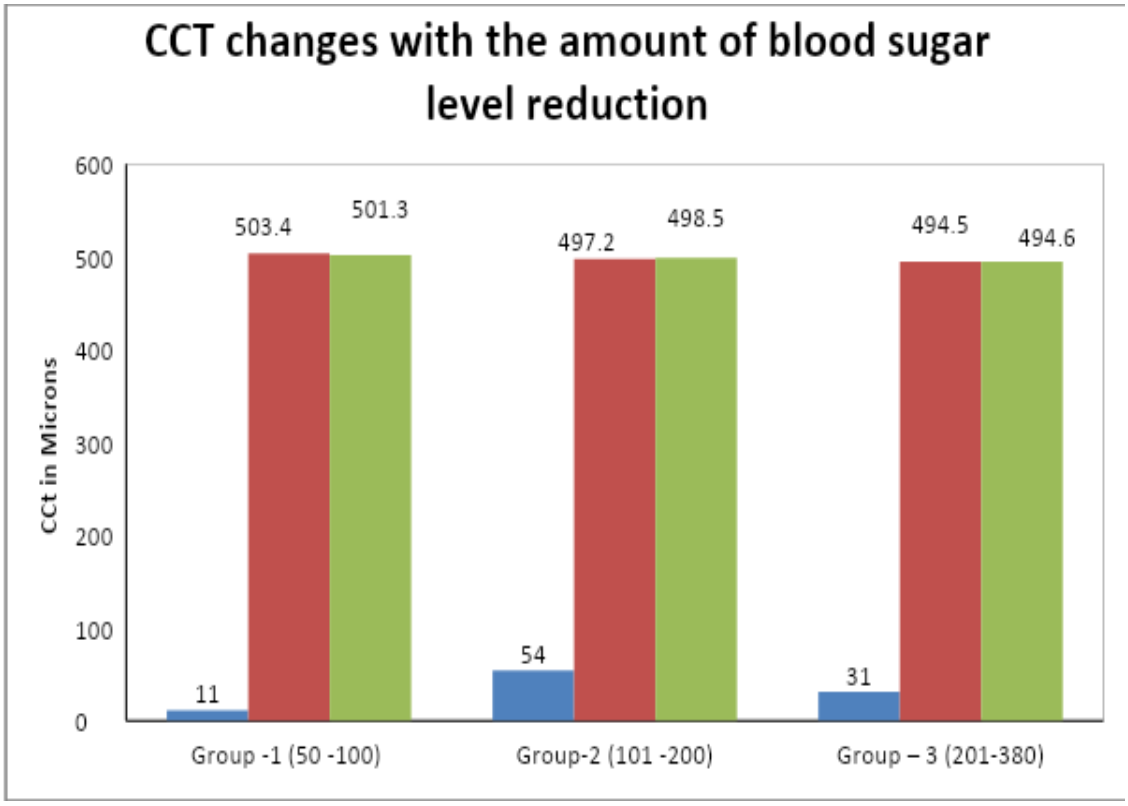


FIG-4: Graph demonstrating CCT changes in relation to Blood sugar level reduction.

Fig 4 demonstrated that there is no statistically significant relationship between the amount of blood sugar level decrease reported in the three groups and changes in CCT values.
Group -1 =50 -100, Group -2 =101 -200, Group- 3 =201 -380.

Table 6: Compare the mean blood sugar level and central corneal thickness value between the change in CCT (Increase, no changes & decrease)

	CCT Changes in microns				F Value	Sig**
Parameter	Group -1 (>5 Microns) 12	Group-2 (1-5 Microns) 28	Group – 3 (No Changes) 14	Group 4 ≤ zero 42		
Hyperglycemia Mean ± SD	297.17 ± 68.10	298.50 ± 55.14	331.00 ± 59.80	309.99± 60.68	1.039	.379(NS)
CCT In Hyperglycemia Mean ± SD	497.01 ± 38.68	498.07 ± 21.9	512.71 ± 27.3	491.64 ± 40.5	1.350	.263 (NS)
Euglycemia Mean ± SD	122.08 ± 17.4	129.54 ± 24.5	129.86 ± 23.6	135.62 ± 26.7	1.048	.375 (NS)
CCT in Euglycemia Mean ± SD	505.67 ± 38.56	500.43 ± 22.16	512.71 ± 27.33	487.57 ± 40.92	2.390	.074(NS)
PPBS difference Mean ± SD	175.08 ± 64.07	168.96 ± 62.13	201.14 ± 58.34	174.12 ± 68.69	.820	.486(NS)

Table 6 showed that there is no statistical significant of mean blood sugar level and CCT in Hyperglycemia and euglycemia between the changes of CCT mentioned in 4 groups (increases, no changes and decreases).

Table 7 :Comparison of the patients mean PPBS and CCT value before and after treatment among male and female patients

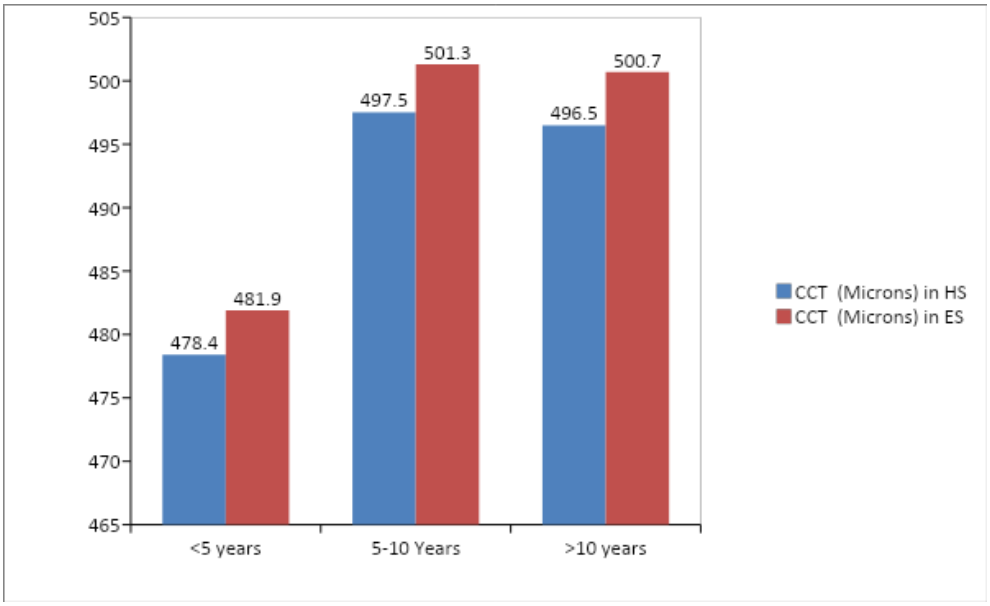
Parameter	Male (27)	Female (69)	F Value	Sig**
Hyperglycemia Mean ± SD	295.37 ± 61.46	312.93 ± 60.14	-1.279	.204(NS)
CCT In Hyperglycemia Mean ± SD	493.26 ± 38.68	498.84 ± 33.8	-.717	.485 (NS)
Euglycemia Mean ± SD	133.19 ± 25.24	138.58 ± 24.66	.462	.645 (NS)
CCT in Euglycemia Mean ± SD	492.96 ± 35.32	498.93 ± 34.59	-.749	.456(NS)
PPBS difference Mean ± SD	162.19 ± 67.15	182.35 ± 63.15	-1.380	.171(NS)
CCT difference Mean ± SD	-.296 ± 5.4	.870 ± 4.3	-.360	.744(NS)

There was no statistical significance between the male and female mean sugar level and CCT thickness before and after treatment of one month

Table 8 : CCT change in subgroups divided as per duration of diabetes

Duration of Diabetes	No. of patients	CCT (Microns) in HS Mean ± SD	CCT (Microns) in ES Mean ± SD	F test	Significance
<5 years	20	478.4 ±5.156	481.79 ±51.482	2.270	.117 (NS)
5-10 Years	45	497.5±2.525	501.39±26.104		
>10 years	31	496.5±3.372	500.74±33.301		

HS- Hyperglycemic state, ES-Euglycemic state



HS- Hyperglycemic state, ES-Euglycemic state

Fig 5 : CCT change in subgroups divided as per duration of diabetes.

DISCUSSION

In India, diabetes is among the most prevalent public health issues.[7] Due to its significance as a gauge of corneal health, CCT measurement has grown to be a crucial ocular parameter.[8]

In order to exclude individuals with slight blood sugar fluctuations, which could not result in any discernible changes in the corneal parameters, we included patients with blood sugar level drops of at least 50 mg/dl as well as blood sugar levels less than 200 mg/dl. Since it was standard practice for diabetic patients to retest their blood sugar levels at one month, we looked for changes at that time.

Patients with renal dysfunction were omitted as well, since their fluid buildup might change the hydration of their corneas. There isn't any research on corneal thickness in diabetics with nephropathy as a distinct population, though.

The 96 participants in the study had mean CCTs of 497.27±34.208 micrometers when they were hyperglycemic and 497.25±35.004 micrometers when they were euglycemic. The CCT did not differ between euglycemic and hyperglycemic conditions.

There were no differences in corneal thickness between hyperglycemic and euglycemic conditions in our research.

We suggest that under typical circumstances, abrupt increases in blood sugar levels do not result in transient alterations in CCT. The cornea in a hyperglycemic state, however, may react differently than in a euglycemic state, under stress

or hypoxia (caused by contact lenses or surgical trauma). Mc Namara et al. observed that diabetics in a hyperglycemic state had less corneal swelling but a longer corneal recovery time than those in a euglycemic state.[9]
Short-term impacts on the cornea's swelling response and recovery time during hypoxic and stressful situations may be clinically significant for individuals undergoing surgery or wearing frequent contact lenses, which may alter CCT in these circumstances.
Hyperglycemia or blood sugar swings are unlikely to result in short-term changes in CCT in typical, non-stressful circumstances.[10] Therefore, hyperglycemia is unlikely to have an impact on routinely monitoring intraocular pressure readings.

CONCLUSION

1. There was no difference in central corneal thickness in diabetics in hyperglycemic and euglycemic state achieved at 1 month.
2. There was no correlation between change in blood sugar levels and change in central corneal thickness.
3. Short term fluctuations (1 month) in blood sugars did not cause any change in CCT in diabetics .
4. Routine IOP measurements are unlikely to be influenced by short term variations in blood sugars in diabetics.

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