Changes in corneal thickness in poorly controlled type-II diabetics after reaching a properly controlled diabetic status

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Purpose
The aim of this study was to evaluate the corneal thickness changes in the uncontrolled diabetics when proper control was achieved.
Design
This is a retrospective, randomized, clinical trial.
Patients and methods
The charts of 198 eyes of 99 uncontrolled diabetic patients (with glycosylated hemoglobin≥7%) were selected using standard random tables. Complete ophthalmologic examination with central corneal thickness (CCT) measurement using the Nidek tonoref III was extrapolated. The glycemic status of the patients was controlled (glycosylated hemoglobin <7%) in a 3-month period. The CCT of all patients was recorded before and after the glycemic control and was compared.
Results
The mean CCT value of the uncontrolled diabetic patients' eyes was 531.38 ±35.56 μm (range=465–602 μm). After achieving the glycemic control, the mean CCT value was 533.95±32.33 μm (range=478–626 μm), with no statistically significant difference (t=–0.524, P=0.601).
Conclusion
The CCT values did not show any significant change in type-II diabetics after their transit from the uncontrolled to the controlled states.

Keywords:
central corneal thickness, cornea, diabetes mellitus, type-II diabetes

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Introduction

Despite being saliently characterized by disturbances in the blood glucose level, yet diabetes mellitus (DM) affects multiple systems of the body. Neuropathy, nephropathy, and retinopathy are the most widely known long-term complications sought in diabetics [1].

Different parts of the eye, in addition to the retina, suffer many alterations due to the long-standing dysglycemic status. Blepharitis, orbital cellulitis, and recurrent hordeola are well-known associations. Iris depigmentation, denervation, neovascularization together with early cataract formation, and secondary glaucoma are famous sight-threatening complications. Transient ametropia with hyperglycemia or hypoglycemia as well as early presbyopia occurrence are also frequently confronted with in diabetics [2–8].

Both structural and physiologic changes, affecting all the corneal layers, have been thoroughly studied and documented among diabetics. These changes were attributed to abnormalities in tear secretion, reduced corneal sensation, and/or inadequate adhesion between the corneal epithelial cells and the epithelial basement membrane. They included superficial punctate keratitis, recurrent corneal erosions, persistent epithelial defects, and corneal endothelial damage [9–12].

The endothelial affection with the consequent alteration in corneal hydration rose a question of whether the corneal thickness would vary with fluctuating levels of blood glucose or the status of diabetic control. Several authors tackled the former and their reports were somewhat contradictory, while the least-tackled issue was the relationship between pachymetric findings and the state of diabetic control as evidenced by the level of glycosylated hemoglobin (HbA1C) [13,14].

This study was conducted to evaluate the corneal thickness changes in the uncontrolled diabetic patients when the glycemic control was achieved.

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Patients and methods

This is a retrospective, randomized clinical trial that included 198 eyes of 99 uncontrolled type-II diabetic patients. The definition of the uncontrolled status was set to having HbA1C level equal to or more than 7%, while reaching a properly controlled status was considered when HbA1C was less than 7%. The inclusion criteria were absence of diabetic neuropathy, nephropathy, as well as free ocular examination with absence of cataract, glaucoma, or diabetic retinopathy changes. Patients with hypertension, serum creatinine more than 1.2 mg%, or patients on insulin therapy were excluded from the study. In addition, patients with previous ocular surgery, patients using rigid gas-permeable contact lenses during the six weeks before ophthalmic examination or soft contact lenses less than 2 weeks before examination, patients with corneal pathology (opacities, dystrophies, degenerations, and ectatic conditions), reduced or absent corneal sensation, ocular surface cicatrization, posterior segment pathologies of the retina and the optic nerve, or patients with uveitis were also excluded from the study.

The study files were selected between January 2021 and December 2021 at the Eye Clinic in the Imperial College London Diabetes Center, United Arab Emirates. The study protocol was based on the tenets of the Declaration of Helsinki and was approved by the Ethics Committee at the Imperial College (on the February 25, 2022 under the batch IREC 076). The Ethical Committee waived the need for a signed informed consent due to the retrospective nature of the study.

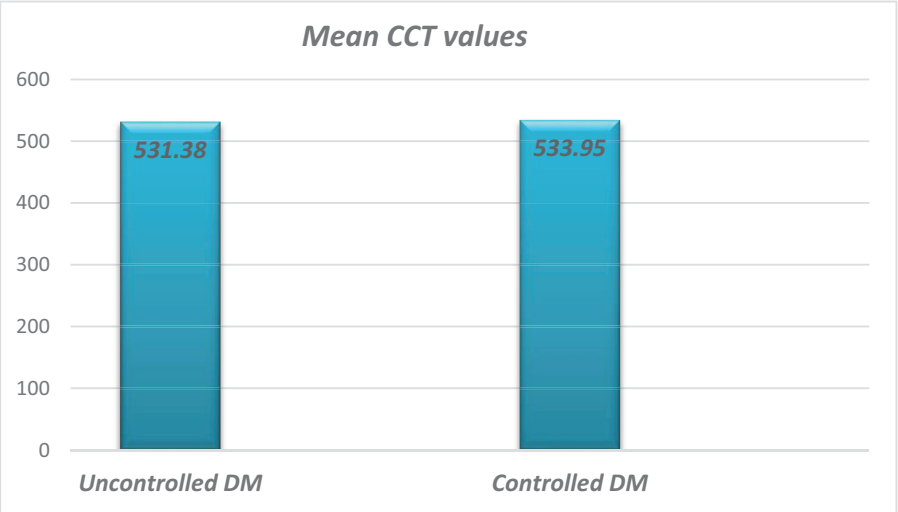
The files of the patients with HbA1C equal to or more than 7% had their detailed ocular and medical history reviewed. A full ophthalmic examination was included using slit-lamp biomicroscopy. Intraocular pressure measurement and biomicroscopic fundus examination were also recorded. The central corneal thickness (CCT) was measured using the Nidek tonoref III (Nidek Co. Ltd, Gamagori, Japan). The patients were then referred to the diabetes clinic for glycemic control and were reviewed 3 months later when their HbA1C had reached the desired value (<7%). Patients failing to reach the desired HbA1C value were given an extra month of follow-up. Failure to achieve diabetic control after this month led to the exclusion of the patient and his substitution with another randomly assigned candidate.

In the follow-up visits, full ophthalmic examination was reperformed together with intraocular pressure measurement and fundus examination. The CCT was also measured.

Statistical analysis

Data analysis was performed using the Statistical Package for Social Sciences (SPSS) software (version 18.0; SPSS Inc., Chicago, Illinois, USA) and Microsoft Excel 2010 (Microsoft Corp., Redmond, Washington, USA). Normality of data was evaluated by the Kolmogorov–Smirnov test. Paired *t* test (for comparisons between the CCT measurements in the uncontrolled versus the controlled diabetic status) was used to assess the statistical significance. The results were considered statistically significant when the *P* value was equal to or less than 0.05.

Figure 1



Mean central corneal thickness in both uncontrolled and controlled diabetic patients. CCT, central corneal thickness; DM, diabetes mellitus.

Results

The study included 99 type-II uncontrolled diabetic patients (49 males and 50 females) with a mean age of 50.1±13.35 years (range=35–80 years) and a mean duration of DM of 7.1±3.33 years. The mean HbA1C at presentation was 10.02±1.23 mg% (range=7.45–12.07%) and became 6.33±0.26% (range=5.9–6.87%) after control.

When still uncontrolled, the recruited diabetic patients' files showed a mean CCT value of 531.38±35.56 um (range=465–602 μm). After achieving control, the mean CCT value was 533.95±32.33 μm (range=478–626 μm), with no statistically significant difference between measurements before and after achieving the diabetic control (t=–0.524, P=0.601, Fig. 1). In addition, there were no statistically significant differences on comparing the mean CCT of the right eyes (t=–0.906, P=0.367) or that of the left eyes (t=–0.077, P=0.938) before and after achieving diabetic control (Table 1).

Discussion

There has been controversy regarding the effect of DM on the different biometric properties of the cornea either on comparing the diabetics to healthy individuals, hyperglycemic to euglycemic patients, controlled to uncontrolled patients, or complicated to noncomplicated cases. The debate took place especially on comparing diabetics to nondiabetics, but little research efforts were exerted when comparing such presumed changes among uncontrolled diabetics when they have reached their properly controlled status [15–32].

In the current study, the CCT of 198 eyes of uncontrolled type-II diabetics was measured and was re-evaluated after reaching appropriate control. The cutoff point was HbA1C of 7% or more for the uncontrolled and less than 7% for the controlled. Reaching the latter value was given a 3 months' period that was extended for another month for patients in whom control was failed to achieve. No significant differences were found between the uncontrolled and controlled conditions of DM in the recruited patients regarding their CCT values.

Table 1 Central corneal thickness in the right and left eyes of the study group in both controlled and uncontrolled diabetics

Eye	Uncontrolled DM Mean±SD	Controlled DM Mean±SD	*P*
Right eyes	531.43±37.48	535.98±32.72	0.367
Left eyes	531.54±34.63	531.92±33.23	0.938
Total eyes	531.38±35.56	533.95±32.33	0.601

DM, diabetes mellitus.

The fact that corneal collagen lamellae are poorly cross-linked, especially in the younger age groups, should favor corneal imbibition of fluids governed by the osmotic influences of hyperglycemia. This, theoretically, should have led to thicker corneas, especially in the uncontrolled cases of the first type of the disease. However, the opposite was found to be true in different studies that provide a logic backup to our findings [14,33]. It is also known that the corneas get gradually cross-linked with aging. Moreover, longer durations of DM are associated with increased levels of advanced glycosylation in the tissues. These substances hypothetically increase the cross-linking of the lamellar corneal collagen resulting in stiffening of the corneal tissues and creating more resistance to swelling and subsequent thickening [33]. Based on this corneal imbibition of fluids, it should be easier in younger ages, especially in early diagnosed cases of type-I DM to get corneal thickening with uncontrolled status. With progress of age and/or longer time of diabetes, corneal swelling due to increased fluid content and, hence, thickening should be more difficult to take place. This also supports the current study results [33].

Desai [15], in his study conducted on 50 type-II diabetics and 50 nondiabetic age-matched controls, reported that the mean CCT values were significantly higher among diabetics. Kim and Kim [16] stated similar results in a larger-scale study on 511 type-II diabetic patients and 900 nondiabetic controls. Qamar-ul-Islam [17], Busted *et al.* [18], and Goldich *et al.* [19] also concluded that diabetics have thicker corneas than nondiabetics. However, the mean CCT among and within different populations lies between 510 and 560 μm, which is a considerably wide range that can result in such significant differences in which DM has no contributing role, especially when most of these studies were conducted on a small number of cases as reported by other authors [20–23], except for the Kim and Kim [16] study.

On the other hand, other studies found no statistically significant differences in CCT values among diabetics and nondiabetics. Adnan *et al.* [23] found no differences between type-I diabetics and normal healthy individuals regarding the CCT. Yuksekkaya *et al.* [24] also found that the CCT values were not significantly different among children with DM of more than 5-year duration when compared with those with less than 5-year duration of the disease.

Canan *et al.* [25] reported that the CCT values did not show any significant differences among diabetics with diabetic retinopathy compared with those without diabetic retinopathy (using three different methods for measuring the corneal thickness: ultrasonography, scanning slit anterior segment imaging, and optical coherence tomography). Sing *et al.* [26], in their study about CCT and its association with ocular and systemic factors in West African population, concluded that no significant association existed between the CCT values and the presence or absence of DM. Nalcacioglu-Yuksekkaya *et al.* [27] stated that DM did not have any effect on the different corneal biomechanical parameters in childhood.

Agreeing with the current study results, George *et al.* [28] reported that there were no significant changes in CCT measurements with varying postprandial blood sugar levels in type-II DM patients. Toygar *et al.* [29] also conducted a more comprehensive study in type-II diabetics in which they concluded that there were no significant differences in CCT measurements between patients without retinopathy compared with patients with retinopathy and in patients with nonproliferative diabetic retinopathy compared with patients with proliferative diabetic retinopathy despite recording thicker corneas in diabetics compared with nondiabetics. On the other hand, Taha *et al.* [30] reported a positive correlation between HbA1C and CCT in the three groups they studied (uncontrolled diabetics, controlled diabetics, and healthy volunteers). Similarly, Altay *et al.* [31] studied type-II diabetics whose HbA1C levels were above 7% and measured their CCT before and after reaching glycemic control (HbA1C <7%). They found a significant difference between the mean CCT values measured (552.3±29.26 vs. 542.36±27.2 μm, respectively, P=0001). Park *et al.* [32] disagreed with them, despite reporting significantly thicker corneas in diabetics, yet they found no significant differences between controlled (HbA1C <7%) and uncontrolled (HbA1C >7%) diabetics regarding their CCT (562.33±34.62 vs. 556.96±29.5 μm, respectively, P=0.567) as well as other corneal biomechanical indices.

Conclusion

The CCT did not show any significant change in type-II diabetics after their transit from the uncontrolled to the controlled states. However, more studies with larger numbers and different types of diabetic patients may still be required to resolve this apparent discrepancy in the results between the different studies.

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Conflicts of interest

There are no conflicts of interest.

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