

Correlation of Central Corneal Thickness with Severity of Diabetic Retinopathy and Glycemic Control in Type 2 Diabetes Mellitus

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Abstract:

Background: Diabetic retinopathy (DR) remains one of the most common microvascular complications of type 2 diabetes mellitus and one of the leading causes of preventable vision loss in the world. In conjunction with systemic factors such as the duration of diabetes and glycemic control, the severity of retinopathy may also be related to eye-specific structural parameters, such as central corneal thickness (CCT). Changes in CCT have been associated with corneal endothelial dysfunction in diabetes, which could also be related to DR progression. Markers of long-term glycemic status, such as HbA1c, provide insights into the aforementioned relationships.

Objective: This study was conducted to correlate central corneal thickness, the severity of diabetic retinopathy and HbA1c in patients with type 2 diabetes mellitus.

Methods: This was a prospective observational study that was performed in the Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India for one year. The study design included total of 128 patients who had type 2 diabetes mellitus. The patients underwent an extensive ophthalmology examination, which included slit lamp examination, fundus examination, and OCT when indicated, and a measurement of central corneal thickness with ultrasound pachymetry. The severity of diabetic retinopathy was graded according to Early Treatment Diabetic Retinopathy Study (ETDRS) classification. HbA1c levels were measured using standardized laboratory methods. CCT, severity of DR, and HbA1c were analyzed statistically.

Results: There was a statistically significant difference in central corneal thickness patients with more advanced stages of diabetic retinopathy than those with no or mild retinopathy. HbA1c was statistically significantly related to both increased corneal thickness and higher severity of diabetic retinopathy. There was a strong correlation between poor glycemic control (HbA1c $\geq 8.0\%$) and corneal thickening, especially in patients diagnosed with proliferative diabetic retinopathy.

Conclusion: Central corneal thickness significantly correlates with both diabetes retinopathy severity and HbA1c in type 2 diabetes patients. CCT may serve as a supplementary parameter to assess reflection of disease progression and systemic control in the ability to manage patients comprehensively across a range of diabetic patients.

Keywords: Type 2 Diabetes Mellitus, Central Corneal Thickness, Diabetic Retinopathy, HbA1c, Glycemic Control, Pachymetry.

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Introduction

Diabetes mellitus (DM), especially type II DM, is a global health issue that continues to increase. Among its numerous systemic complications, ocular involvement remains a significant source of morbidity. Diabetic retinopathy (DR) is a well-known major cause of visual impairment and blindness around the world [1]. The severity of DR is influenced by a variety of factors, including duration of diabetes, glycemic control, blood pressure, and lipids levels. More recently, changes

in the anterior segment of the eye, especially the cornea, has become of interest as potential markers of diabetes progression [2].

The cornea is avascular and depends on the corneal endothelium to maintain corneal thickness and transparency. Microvascular changes from chronic hyperglycemia will affect the cornea, especially its transparency and edematous state [3]. Central corneal thickness (CCT) is a clinically significant

measurement in potentially diagnosing corneal pathologies or gauging severity for treatment-related decisions in glaucoma management or corneal refractive surgery. Changes in CCT have been reported in patients with diabetes, where patients with thicker corneas may have dysfunctional corneal endothelium, perhaps caused by changes in control of corneal hydration, and more advanced stages of diabetes. These corneal changes may also correlate with severity of DR making CCT a potential surrogate marker of ocular and systemic overall burden of disease [4]. Glycosylated hemoglobin (HbA1c) is a well-established good marker of long-term glycemic control reflecting average blood glucose levels over the past 8–12 weeks. Increases in HbA1c have been related to important associations with microvascular complications such as retinopathy, nephropathy, and neuropathy. Additionally, specifically, HbA1c levels related to CCT, and severity of diabetes retinopathy, may be helpful to understanding the relationship between systemic metabolic control of glucose, and ocular structural changes and diabetes. [5].

Although many research studies have been published regarding diabetic retinopathy, there has been relatively little research examining direct correlations between central corneal thickness and the severity of DR and HbA1c levels in patients with type 2 diabetes. A correlation between those characteristics could benefit clinical practice by providing ophthalmologists with one more non-invasive characteristics to assess their disease states. Additionally, this could lead to better identification of patients a higher risk for advanced retinopathy, and potential for earlier treatment and better systemic management.

Therefore, the aim of the current study was to assess the correlation of central corneal thickness to the severity of diabetic retinopathy and the HbA1c levels in patients with type 2 diabetes mellitus. Through the evaluation of these relationships, the current study aims to determine if CCT can be considered an additional adjunctive tool in assessing the complexity of the diabetic patients.

Materials and Methods

Study design and setting: This prospective observational study was conducted based in a hospital, specifically in the Department of Ophthalmology, Patna Medical College and Hospital, Patna, Bihar, India for one year.

Sample Size: A total of 120 patients were enrolled in the study, which was deemed appropriate to provide adequate statistical power while remaining feasible for a single-center prospective analysis. Patients were selected using consecutive sampling based on eligibility criteria.

Inclusion Criteria

1. Patients diagnosed with type 2 diabetes mellitus.
2. Age between 30 and 70 years.
3. Patients willing to provide informed consent and undergo complete ophthalmic and systemic evaluation.

Exclusion Criteria

1. Patients with ocular conditions that may independently affect corneal thickness, such as keratoconus, glaucoma, corneal dystrophies, or prior ocular surgery.
2. Presence of active ocular infection or inflammation.
3. Patients with systemic conditions other than diabetes known to affect corneal morphology (e.g., connective tissue disorders).
4. History of contact lens use within the last six months.

Methodology

Following informed consent, a detailed history and systemic evaluation of each participant was then performed including duration of diabetes, current treatment, and comorbidities. The HbA1c test was done with standard laboratory workup and results expressed in percentage form. Patients were categorized by HbA1c levels in the following categories: Well controlled $\leq 7.0\%$, moderately controlled 7.1–9.0%, and poorly controlled $> 9.0\%$.

All patients underwent a comprehensive ophthalmic evaluation including best-corrected visual acuity, slit-lamp biomicroscopy, intraocular pressure, and dilated fundus examination with indirect ophthalmoscopy and fundus photographs. The degree of diabetic retinopathy was graded by the Early Treatment Diabetic Retinopathy Study (ETDRS) classification of no retinopathy, mild non-proliferative, moderate non-proliferative, severe non-proliferative, and proliferative diabetic retinopathy.

Central corneal thickness (CCT) was measured via ultrasonic pachymetry of which five consecutive readings were recorded for each eye and the mean reading was used for analysis. Only right eyes were used to obtain inter-eye variability.

Data Analysis: The gathered data was entered into and analyzed using appropriate statistical software. Descriptive statistics were used to analyze baseline demographic and clinical characteristics. One-way analysis of variance (ANOVA) was used to assess mean CCT values among levels of DR severity and categories of HbA1c. Pearson's correlation coefficient was used to examine the relationship between CCT, severity of DR, and HbA1c. A p-value of < 0.05 was considered statistically significant.

Results

The study consisted of a total of 120 patients who were diagnosed with type 2 diabetes mellitus. The mean age of the study participants was 54.2 years, while males were slightly more prevalent. The mean duration of diabetes was 10.8-years. The types of HbA1c levels were 34.1% well controlled, 40.8%

moderately controlled and 25% poorly controlled. Diabetic retinopathy (DR) was noted in 78 (65%) diabetic patients, which corresponded with the severity grades in the ETDRS classification. The mean central corneal thickness (CCT) gradually rose with the severity DR and HbA1c levels. Findings follow in the upcoming tables.

Table 1: Age-wise distribution of study participants

Age group (years)	Number of patients	Percentage (%)
30–40	18	15.0
41–50	27	22.5
51–60	44	36.7
61–70	31	25.8

Table 2: Gender distribution of study participants

Gender	Number of patients	Percentage (%)
Male	68	56.7
Female	52	43.3

Table 3: Duration of diabetes among study participants

Duration of diabetes (years)	Number of patients	Percentage (%)
<5	24	20.0
5–10	38	31.7
11–15	41	34.2
>15	17	14.1

Table 4: Distribution of patients based on HbA1c levels

HbA1c category (%)	Number of patients	Percentage (%)
≤7.0 (Well controlled)	41	34.1
7.1–9.0 (Moderately controlled)	49	40.8
>9.0 (Poorly controlled)	30	25.0

Table 5: Distribution of patients based on diabetic retinopathy status

Retinopathy status	Number of patients	Percentage (%)
No retinopathy	42	35.0
Retinopathy present	78	65.0

Table 6: Distribution of patients by severity of diabetic retinopathy

DR severity (ETDRS)	Number of patients	Percentage (%)
Mild NPDR	19	15.8
Moderate NPDR	28	23.3
Severe NPDR	17	14.2
Proliferative DR	14	11.7

Table 7: Mean central corneal thickness in different DR categories

DR severity	Mean CCT (μm) ± SD
No DR	532.4 ± 12.6
Mild NPDR	541.2 ± 14.8
Moderate NPDR	547.8 ± 16.1
Severe NPDR	553.6 ± 18.2
Proliferative DR	559.4 ± 20.5

Table 8: Comparison of mean CCT among HbA1c groups

HbA1c group	Mean CCT (μm) ± SD
≤7.0	533.6 ± 13.2
7.1–9.0	544.8 ± 15.7
>9.0	555.1 ± 18.4

Table 9: Correlation between HbA1c levels and central corneal thickness

Correlation	r-value	p-value
HbA1c vs CCT	+0.71	<0.001

Table 10: Correlation between DR severity and central corneal thickness

Correlation	r-value	p-value
DR severity vs CCT	+0.66	<0.001

Table 11: Association between duration of diabetes and central corneal thickness

Duration of diabetes (years)	Mean CCT (μm) $\pm$ SD
<5	530.2 $\pm$ 11.5
5–10	540.6 $\pm$ 14.2
11–15	548.7 $\pm$ 16.0
>15	556.2 $\pm$ 18.9

Table 12: Multivariate regression analysis of factors associated with CCT

Factor	Beta coefficient	p-value
HbA1c	+0.52	<0.001
DR severity	+0.44	<0.001
Duration of diabetes	+0.21	0.031
Age	+0.08	0.112

Table 1 demonstrated that the majority of patients were between 51 and 60 years of age. Table 2 showed a slight male predominance. Table 3 indicated that over half of the participants had diabetes for more than 10 years. Table 4 revealed that most patients belonged to the moderately controlled HbA1c group. Table 5 highlighted that diabetic retinopathy was present in two-thirds of the study sample. Table 6 showed moderate non-proliferative DR as the most common grade. Table 7 demonstrated that CCT increased progressively with DR severity. Table 8 indicated that poorly controlled diabetes was associated with thicker corneas. Table 9 revealed a strong positive correlation between HbA1c levels and CCT. Table 10 showed a significant correlation between DR severity and CCT. Table 11 highlighted that longer duration of diabetes was linked to higher mean CCT values. Table 12 confirmed through multivariate regression that HbA1c and DR severity were independent predictors of corneal thickening.

Overall, the results indicate that central corneal thickness is significantly associated with both glycemic control and severity of diabetic retinopathy, suggesting its potential role as an adjunctive marker for disease monitoring in type 2 diabetes mellitus.

Discussion

In the present study, the authors sought to examine the relationship between central corneal thickness (CCT) and severity of diabetic retinopathy (DR) and glycemic control, as measured by hemoglobin A1c (HbA1c), in subjects with type 2 diabetes mellitus [6]. Results showed HbA1c levels had a significant relationship with worse severity of DR and diabetes duration, as well as an increase in CCT level. These results are consistent with other literature and suggest that microvascular pathology from diabetes impacts the retina and corneal integrity, which is significant because it suggests that corneal parameters may be a surrogate for systemic disease

burden [7]. The finding of increased CCT with an increase DR severity has clinical significance. For instance, mean CCT was within an expected physiological range in subjects without retinopathy, while CCT was significantly elevated for patients with proliferative retinopathy [8]. Therefore, in tandem, the findings support that both CCT increases as a clinical finding and corneal endothelial dysfunction occurs from microangiopathy in adult subjects with diabetes that likely has an impact of the cornea to maintain the proper hydration in the stroma. Lastly, since CCT continues to increase with worse DR severity, both retinal vascular impairment and corneal endothelial impairment may be linked pathophysiologically [9]. Similarly, HbA1c was found to be a strong correlate of CCT, which reconfirms our understanding of HbA1c as a measure of long-term glycemic control. Patients that had poorly controlled diabetes (HbA1c >9.0%) had the thickest corneas while the better controlled patients had the closest CCT to normal values [10]. Thus, as stated earlier, these finding highlights how imperative strict glycemic control is not only for prevention of retinopathy but also for the health of the cornea. This further supports the interpretation of suboptimal overall metabolic control to some extent does have a direct effect on corneal morphology as evidenced CCT, may be a clinically relevant parameter to assess overall diabetes control [11]. In addition, duration of diabetes was a statistically significant variable in relation to CCT where patients with greater than 15 years of diabetes had significantly thicker corneas than patients without long duration diabetes. This finding supports the cumulative effect of chronic hyperglycemia, and long duration of microvascular insult on corneal health which also relates to the progressive nature of diabetic complications [12].

Clinically, these implications are noteworthy; raising CCT in patients could impact intraocular pressure assessments and CCT might lead to an underestimate of glaucoma risk, in the event that it

is ignored [13]. Furthermore, any corneal structural alterations may also be relevant for the consideration of refractive results in diabetic patients undergoing keratorefractive procedures like LASIK or cataract procedures. Therefore, it is important for the ophthalmologist to recognize such modifications in care delivery for diagnostic assessment and surgical intervention [14]. The multivariate regression results of the positive independent predictive roles of HbA1c and DR severity on CCT also provide additional evidence for the hypothesis for CCT to provide a complimentary measure in diabetic ocular screening. While the fundus examination is considered the gold standard for DR assessment, the pachymetric assessment of CCT could provide an additional ancestral measure of disease severity or systemic metabolic status [15]; an extra measure of value in locations where limitations to effective resource allocation create an urgency and need for non-invasive and / or non-resource demanding identification of at-risk patients early and rapidly.

While the results of this study support the greater recognition of ocular sequelae of systemic diabetes, the results should be cautiously interpreted, as corneal thickness (CT) measurements can be variably influenced by age, ethnicity or other coexisting ocular disease-related factors, which will require larger multi-centered studies to evaluate. The current study indicates that CT increases in severity with diabetic retinopathy, poor glycemic control, and longer duration of diabetes. Therefore, CT may also be a useful, non-invasive adjunctive measure to provide a more comprehensive and objective assessment of patients with diabetes. Involving CT in routine management could also improve early detection of risk for more advanced disease, therefore provide specificity to better counsel patients, and ultimately improve management of the disease in clinical practice.

Conclusion

Overall, the present study shows that CCT is significantly correlated with DR severity and glycemic control in patients with Type 2 diabetes mellitus. Patients with diabetic retinopathy and understood poor glycemic control in relation to HbA1c levels had significantly thicker corneas than patients with no retinopathy and in better glycemic control. Additionally, diabetes duration was associated with progressive corneal thickening, suggesting that chronic hyperglycemia has a cumulative impact on corneal morphology. Such findings suggest that CCT may be beneficial as a valuable adjunct clinical marker in the assessment of diabetic patients. Implementing pachymetry methods into the clinic by ophthalmologists may give additional information in assessing severity, predicting progression, and establishing a management plan in diabetic patients. This is especially important for patients who undergo

procedures where precise corneal measurements are necessary, like glaucoma assessment, refractive surgery, or cataract surgery.

In summary, strict metabolic control and routine eye care are crucial for complex management of diabetes. CCT assessment with standard retinal assessment may increase the clinical awareness of at-risk patients and improve longer term visual outcomes of individuals diagnosed with Type 2 diabetes mellitus.

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