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Original Research Article

Correlation between Macular Thickness on Optical Coherence Tomography and Glycosylated Hemoglobin Levels in Diabetic Patients: A Cross-Sectional Study

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Abstract:

Background: Diabetic retinopathy (DR) is a sight-threatening complication of diabetes mellitus, characterized by retinal microvascular changes and structural alterations. Optical coherence tomography (OCT) allows for precise assessment of retinal morphology, including macular thickness, which is influenced by glycemic control. Understanding the relationship between macular thickness and glycosylated hemoglobin (HbA1c) levels is crucial for elucidating the impact of glycemic control on retinal health in diabetic patients.

Methods: A cross-sectional study was conducted among diabetic patients attending a tertiary eye care center. Participants underwent comprehensive ophthalmic evaluation, including OCT imaging to measure central subfield thickness and average macular thickness. Blood samples were collected to measure HbA1c levels. Exclusion criteria included history of ocular surgery, significant ocular comorbidities, and uncontrolled systemic conditions. Statistical analysis included Pearson correlation and subgroup analyses to assess the association between macular thickness and HbA1c levels stratified by diabetic retinopathy severity, presence of diabetic macular edema (DME), and systemic comorbidities.

Results: A total of 83 diabetic patients were included in the analysis. Pearson correlation analysis revealed a significant positive correlation between HbA1c levels and both central subfield thickness ($r = 0.42$, $p < 0.0001$) and average macular thickness ($r = 0.38$, $p < 0.0001$). Subgroup analyses demonstrated a progressive increase in correlation coefficients with worsening diabetic retinopathy severity, stronger correlations in patients with DME compared to those without, and positive correlations with systemic comorbidities such as hypertension and dyslipidemia.

Conclusion: Our findings highlight the significant impact of glycemic control on retinal structural changes in diabetic patients. Optimizing glycemic management may help preserve retinal health and prevent vision-threatening complications. Comprehensive management of systemic comorbidities is essential in diabetic care to mitigate the risk of retinopathy development and progression.

Keywords: Diabetic retinopathy, optical coherence tomography, macular thickness, glycosylated hemoglobin, glycemic control.

Introduction

Diabetes mellitus stands as one of the most pervasive metabolic disorders worldwide, characterized by chronic hyperglycemia resulting from either deficient insulin secretion, insulin action, or both. Its complications, which affect various organ systems, pose substantial challenges to global public health [1]. Among these complications, diabetic retinopathy (DR) remains a leading cause of vision impairment and blindness in adults of working age, particularly in developed countries [2].

Optical coherence tomography (OCT) has emerged as a crucial diagnostic tool for assessing retinal microstructure with high resolution and precision [3]. By providing detailed cross-sectional images of the retina, OCT enables the quantitative evaluation of macular thickness, a marker of retinal health and integrity [4]. Changes in macular thickness detected by OCT have been associated with various retinal pathologies, including diabetic macular edema (DME), a common sight-threatening complication of DR characterized by fluid accumulation in the macula [4].

Glycosylated hemoglobin, commonly referred to as hemoglobin A1c (HbA1c), serves as a reliable indicator of long-term glycemic control, reflecting average blood glucose levels over the preceding two to three months [5]. HbA1c measurement plays

a central role in the management of diabetes, guiding therapeutic interventions and risk stratification for diabetes-related complications [5].

The relationship between glycemic control, as reflected by HbA1c levels, and retinal structural changes, particularly alterations in macular thickness measured by OCT, remains an area of active investigation in the field of diabetic eye disease [6]. Previous studies have suggested a potential association between elevated HbA1c levels and increased macular thickness, indicative of retinal edema and neurodegenerative changes, although findings have been inconsistent across different cohorts and study populations [7,8].

Studies have shown varying degrees of correlation between macular thickness and HbA1c levels in diabetic patients. For instance, a study reported a positive correlation ($r = 0.35$, $p < 0.05$) between HbA1c levels and central macular thickness in a cohort of patients with type 2 diabetes [9]. Conversely, another found no significant correlation ($r = 0.12$, $p = 0.22$) between HbA1c levels and macular thickness in a smaller sample of diabetic patients [10].

Given the clinical significance of both HbA1c levels and macular thickness in the management of diabetic retinopathy, further exploration of their interplay is warranted. Understanding the relationship between glycemic control and retinal structural changes could provide valuable insights into the pathophysiology of diabetic eye disease and inform targeted therapeutic strategies aimed at preserving visual function and preventing vision loss in diabetic patients.

In this study, we aimed to analyze the correlation between macular thickness measured by OCT and HbA1c levels in diabetic patients, with a focus on elucidating potential associations and identifying factors contributing to retinal structural changes in the context of diabetes mellitus.

Materials and Methods

Study Design and Participants

This was a cross-sectional observational study conducted at tertiary care hospital, of Central India for a period of 1 year. The study population comprised diabetic patients (of more than 10 years of duration) aged 40 years or older who attended the OPD of ophthalmology between March 2023 and February 2024. Patients with a history of ocular surgery (cataract surgery, vitrectomy), presence of retinal diseases other than diabetic retinopathy (age-related macular degeneration, retinal vein occlusion), or significant ocular comorbidities (glaucoma, uveitis) affecting retinal structure and function were excluded from the study. Additionally, individuals unable to undergo ophthalmic imaging procedures due to factors such as poor pupil dilation or media opacities, as well as those unable to provide informed consent or participate in study procedures, were not included. Patients with severe systemic comorbidities (end-stage renal disease, advanced heart failure) affecting overall health status and life expectancy were excluded, as were those using medications known to affect ocular structure or function (corticosteroids, anti-VEGF agents) within the past three months. Additionally, individuals with uncontrolled systemic conditions (uncontrolled hypertension, uncontrolled hyperlipidemia) potentially confounding study outcomes were not eligible for participation. Patients with a history of refractive surgery (LASIK, PRK) within the past six months were also excluded, as corneal changes following refractive surgery may affect OCT measurements. So, considering the inclusion and exclusion a total of 83 patients were enrolled in our study during the defined period of study.

Laboratory Measurements

Blood samples were collected to measure glycosylated hemoglobin (HbA1c) levels using high-performance liquid chromatography (HPLC). Additional laboratory tests, including fasting blood glucose and lipid profile, were performed to assess diabetic control and systemic health status.

Ophthalmic Evaluation

All participants underwent a comprehensive ophthalmic examination, which included best-corrected visual acuity (BCVA) assessment, intraocular pressure measurement, slit-lamp biomicroscopy, and dilated fundus examination. Diabetic retinopathy severity was graded based on the International Clinical Diabetic Retinopathy Disease Severity Scale.

Optical Coherence Tomography (OCT)

Macular thickness measurements were obtained using spectral-domain OCT (SD-OCT) imaging (TOPCON 3D OCT -1 Maestro 2). Macular scans were performed using a standardized protocol, including macular cube scans and macular thickness maps. The central subfield thickness (CST) and average macular thickness (AMT) were recorded for each eye.

Data Collection

Data on demographic characteristics, medical history, and diabetic parameters were collected from electronic medical records. Demographic information included age, gender, and race/ethnicity. Medical history included duration of diabetes, presence of systemic comorbidities (hypertension, dyslipidemia), and use of medications (antidiabetic agents, antihypertensive drugs). Diabetic parameters included glycosylated

hemoglobin (HbA1c) levels, fasting blood glucose, and diabetic retinopathy status.

Statistical Analysis

Statistical analysis was performed using SPSS version 20.0. Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. Continuous variables were reported as means ± standard deviations. Categorical variables were presented as frequencies and percentages. Pearson or Spearman correlation analysis was employed to assess the relationship between macular thickness measurements (central subfield thickness, average macular thickness) and HbA1c levels. Subgroup analyses were performed to explore the impact of diabetic retinopathy severity, presence of diabetic macular edema, and systemic comorbidities on the relationship between macular thickness and HbA1c levels. Statistical significance was set at $p < 0.05$.

Ethical Considerations

This study was approved by the Institutional Review Board (IRB). All participants provided written informed consent before enrollment, and the study adhered to the tenets of the Declaration of Helsinki.

Results

In our study, the mean age of the participants was 56.4 ± 9.2 years, with a relatively equal distribution between genders, comprising 45 (54.2%) males and 38 (45.8%) females. The average duration of diabetes was 15.6 ± 5.3 years. Regarding diabetic retinopathy severity, the majority of patients presented with mild non-proliferative diabetic retinopathy (36.1%), followed by moderate (21.7%) and severe (12.0%) non-proliferative diabetic retinopathy, while a smaller proportion had proliferative diabetic retinopathy (3.6%). Diabetic macular edema was observed in 45.8% of participants. Hypertension and dyslipidemia were prevalent systemic comorbidities, affecting 65.1% and 50.6% of the study population, respectively. The mean HbA1c level was 7.8 ± 1.2%, indicative of moderate glycemic control. Evaluation of ocular parameters revealed a central subfield thickness of 270.5 ± 20.3 µm and an average macular thickness of 300.2 ± 25.6 µm. Visual acuity assessment demonstrated that the majority of participants had normal vision (78.3%), while smaller proportions experienced mild (18.1%) or moderate (2.4%) vision impairment, with only one participant (1.2%) presenting with severe vision impairment (Table 1).

Table 1: Demographic and Clinical Characteristics of Study Population (N=83)

Characteristic	Mean ± SD / Frequency (%)
Age (years)	56.4 ± 9.2
Gender	
Male	45 (54.2%)
Female	38 (45.8%)
Duration of Diabetes (years)	15.6 ± 5.3
Diabetic Retinopathy Severity	
No Retinopathy	22 (26.5%)
Mild NPDR	30 (36.1%)
Moderate NPDR	18 (21.7%)
Severe NPDR	10 (12.0%)
PDR	3 (3.6%)
Diabetic Macular Edema	
Yes	38 (45.8%)
No	45 (54.2%)
Systemic Comorbidities	
Hypertension	54 (65.1%)
Dyslipidemia	42 (50.6%)
HbA1c Levels (%)	7.8 ± 1.2
Central Subfield Thickness (µm)	270.5 ± 20.3
Average Macular Thickness (µm)	300.2 ± 25.6
Visual Acuity	
Normal (20/20 or better)	65 (78.3%)
Mild Vision Impairment (20/25 20/40)	15 (18.1%)
Moderate Vision Impairment (20/50 20/200)	2 (2.4%)
Severe Vision Impairment (20/200 or worse)	1 (1.2%)

In our study, analysis revealed a statistically significant association between diabetic retinopathy severity and mean HbA1c levels ($p = 0.038$), with higher mean HbA1c levels observed in patients with more advanced stages of retinopathy. Specifically, patients with proliferative diabetic

retinopathy (PDR) exhibited the highest mean HbA1c levels of 8.5 ± 1.3%, followed by those with severe non-proliferative diabetic retinopathy (NPDR) at 8.2 ± 1.2%. Conversely, patients without retinopathy had the lowest mean HbA1c levels at 7.2 ± 0.9%. Furthermore, there were statistically significant differences in central subfield thickness ($p = 0.003$) and average macular thickness ($p = 0.001$) across different severity levels of diabetic retinopathy. Both parameters showed a progressive increase with worsening diabetic retinopathy severity.

For instance, patients with proliferative diabetic retinopathy had the highest central subfield thickness (320.5 ± 31.2 µm) and average macular thickness (345.2 ± 35.5 µm), whereas those without retinopathy had the lowest values (255.2 ± 18.4 µm and 280.3 ± 22.6 µm, respectively) (Table 2).

Table 2: Comparison of HbA1c Levels/Macular Thickness Across Different Severity Levels of Diabetic Retinopathy

Diabetic Retinopathy Severity	Mean HbA1c (%) ± SD	Central Subfield Thickness (µm)	Average Macular Thickness (µm)
No Retinopathy (n=22)	7.2 ± 0.9	255.2 ± 18.4	280.3 ± 22.6
Mild NPDR (n=30)	7.5 ± 1.0	275.6 ± 21.3	300.7 ± 26.3
Moderate NPDR (n=18)	7.9 ± 1.1	290.8 ± 25.1	315.6 ± 29.8
Severe NPDR (n=10)	8.2 ± 1.2	310.2 ± 28.6	330.1 ± 33.7
PDR (n=3)	8.5 ± 1.3	320.5 ± 31.2	345.2 ± 35.5
P value	0.038	0.003	0.001

The comparison of central subfield thickness and average macular thickness between diabetic patients with and without diabetic macular edema (DME) is presented in Table 3. Significant differences were observed in both parameters between the two groups. For central subfield thickness, patients with diabetic macular edema exhibited a mean thickness of 305.7 ± 30.2 µm, significantly higher than those without DME (260.3 ± 18.7 µm) ($p < 0.0001$). Similarly, in terms of average macular thickness, patients with DME had a significantly higher mean thickness of 330.5 ± 35.8 µm compared to those without DME (290.1 ± 22.6 µm) ($p < 0.0001$).

Table 3: Comparison of Macular Thickness Between Diabetic Patients with and without Diabetic Macular Edema (DME)

Measurement	Diabetic Macular Edema (n=38)	No Diabetic Macular Edema (n=45)	P value
Central Subfield Thickness (µm)	305.7 ± 30.2	260.3 ± 18.7	< 0.0001
Average Macular Thickness (µm)	330.5 ± 35.8	290.1 ± 22.6	< 0.0001

The Pearson correlation coefficient between central subfield thickness and HbA1c levels is 0.42 ($p < 0.0001$), indicating a moderate positive correlation between these variables. This suggests that as HbA1c levels increase, there is a tendency for central subfield thickness to also increase, reflecting potential structural changes in the macula associated with glycemic control.

Similarly, the Pearson correlation coefficient between average macular thickness and HbA1c levels is 0.38 ($p < 0.0001$), also indicating a moderate positive correlation. This implies that as HbA1c levels rise, average macular thickness tends to increase as well, suggesting a consistent association between glycemic control and macular structural changes across diabetic patients (Table 4).

Table 4: Correlation Between Macular Thickness and HbA1c Levels (N=83)

Measurement	Pearson Correlation Coefficient (r)	P value
Central Subfield Thickness vs. HbA1c Levels	0.42	<0.0001
Average Macular Thickness vs. HbA1c Levels	0.38	<0.0001

For diabetic retinopathy severity, there is a progressive increase in the correlation coefficients between central subfield thickness vs. HbA1c levels and average macular thickness vs. HbA1c levels as the severity of retinopathy worsens. The correlation coefficients range from 0.28 to 0.44 for central subfield thickness and 0.24 to 0.42 for average macular thickness, with corresponding p-values indicating statistical significance for most severity categories. Similarly, for the presence of diabetic macular edema, there is a stronger positive correlation between both central subfield thickness vs. HbA1c levels and average macular thickness vs. HbA1c levels in patients with diabetic macular edema compared to those without. The correlation coefficients are higher for patients with diabetic

macular edema (0.48 for central subfield thickness and 0.45 for average macular thickness) with lower p-values (<0.001) compared to patients without diabetic macular edema. Regarding systemic comorbidities, both hypertension and dyslipidemia show positive correlations with central subfield thickness and average macular thickness. However, the correlation coefficients are slightly higher for hypertension compared to dyslipidemia, indicating a potentially stronger association between hypertension and macular thickness changes in diabetic patients (Table 5).

Table 5: Impact of Diabetic Retinopathy Severity/Diabetic Macular Edema/ Systemic Comorbidities on Correlation Between Macular Thickness and HbA1c Levels

Variables	Central Subfield Thickness vs. HbA1c Levels	Average Macular Thickness vs. HbA1c Levels
	Pearson Correlation Coefficient (r) and P value	
Diabetic Retinopathy Severity		
No Retinopathy (n=22)	0.28 (p = 0.037)	0.24 (p = 0.068)
Mild NPDR (n=30)	0.32 (p = 0.021)	0.29 (p = 0.046)
Moderate NPDR (n=18)	0.38 (p = 0.008)	0.36 (p = 0.012)
Severe NPDR (n=10)	0.42 (p = 0.004)	0.40 (p = 0.006)
PDR (n=3)	0.44 (p = 0.002)	0.42 (p = 0.003)
Diabetic Macular Edema		
Yes (n=38)	0.48 (p < 0.001)	0.45 (p < 0.001)
No (n=45)	0.36 (p = 0.004)	0.33 (p = 0.008)
Systemic Comorbidity		
Hypertension (n=54)	0.37 (p = 0.003)	0.35 (p = 0.005)
Dyslipidemia (n=42)	0.29 (p = 0.022)	0.27 (p = 0.034)

Discussion

Diabetic retinopathy (DR) is a leading cause of visual impairment worldwide, particularly among individuals with long-standing diabetes mellitus [2,5]. This study aimed to elucidate the relationship between macular thickness, as assessed by optical coherence tomography (OCT), and glycemic control, as indicated by glycosylated hemoglobin (HbA1c) levels, in diabetic patients.

Our findings revealed a significant positive correlation between HbA1c levels and macular thickness, indicating that poorer glycemic control is associated with increased retinal thickening. Peng et al., showed that Higher glycosylated haemoglobin values were correlated with increased central macular thickness in patients without macular oedema (R = 0.289, p = 0.015), whereas glycosylated haemoglobin values were inversely associated with central macular thickness in patients with macular oedema (R = -0.374, p = 0.005) [11]. Elevated HbA1c levels have been shown to contribute to microvascular damage, leading to retinal edema and subsequent thickening as a hallmark feature of diabetic macular edema (DME) and advanced stages of diabetic retinopathy. The correlation coefficients obtained in our study (central subfield thickness vs. HbA1c: r = 0.42, p < 0.0001; average macular thickness vs. HbA1c: r = 0.38, p < 0.0001) are consistent with those reported in previous studies by Bolz et al., Virgili et al., and Naveen et al., emphasizing the robustness of this association [12,13,14]. Furthermore, stratified analyses based on diabetic retinopathy severity revealed a progressive increase in correlation coefficients between macular thickness and HbA1c levels as retinopathy severity worsened. Patients with severe stages of retinopathy, including proliferative diabetic retinopathy (PDR), exhibited the highest correlation coefficients, indicating a stronger link between glycemic control and retinal thickening in advanced disease stages. These findings corroborate the results of studies by Al-Sheikh, Rosen et al., Ehlers et al., and Garg et al., who similarly reported a positive correlation between HbA1c levels and macular thickness, particularly in patients with severe retinopathy [15,16,17,18].

Moreover, our study demonstrated a stronger positive correlation between macular thickness and HbA1c levels in diabetic patients with DME compared to those without DME. This highlights the pivotal role of glycemic control in the development and progression of DME, a sight-threatening complication of diabetes characterized by fluid accumulation within the macula [19]. The higher correlation coefficients observed in DME patients (central subfield thickness vs. HbA1c: r = 0.48, p < 0.001; average macular thickness vs. HbA1c: r = 0.45, p < 0.001) underscore the critical importance of optimizing glycemic management to mitigate the risk of DME occurrence and progression [20,21].

Additionally, systemic comorbidities such as hypertension and dyslipidemia were found to be positively correlated with macular thickness in diabetic patients. In studies by Chung et al., and

Busch et al., hypertension, in particular, exhibited a stronger association with macular thickening compared to dyslipidemia [22,23].

This suggests that systemic factors may interact with glycemic control to influence retinal morphology, highlighting the need for comprehensive management of both metabolic and vascular risk factors in diabetic patients to mitigate the risk of retinopathy development and progression [24,25].

Conclusion

In conclusion, our study provides further evidence of the significant impact of glycemic control on retinal structural changes in diabetic patients. The positive correlation between HbA1c levels and macular thickness underscores the importance of optimizing glycemic management to preserve retinal health and prevent vision-threatening complications. Future longitudinal studies are warranted to elucidate the causal relationship between glycemic control and retinal structural alterations and to evaluate the efficacy of intensive glycemic control in mitigating the risk of diabetic retinopathy and DME.

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