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Original Article

CORRELATION BETWEEN HBA1C LEVEL AND THICKNESS OF BOTH MACULA AND CHOROID IN PATIENTS WITH TYPE II DIABETES MELLITUS

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Abstract

Background: *Diabetic retinopathy is the most common cause of visual impairment and the primary cause of blindness in individuals of working age. Swept source OCT enhances the ability to visualize the retina and choroid in a single image. The average plasma glucose concentration over extended periods and the long-term management of hyperglycemia are determined by measuring glycated hemoglobin (HbA1c).* ***Aim:*** *To test the relationship between HbA1c levels and both central macular thickness and subfoveal choroidal thickness in patients with type II DM using SS-OCT.* ***Methods:*** *This comparative, non-interventional cross-sectional study comprised 90 eyes of 49 adult patients, assigned to three groups based on their HbA1c. Group 1 had inadequate glycemic control (HbA1c >7%), Group 2 had good glycemic control (HbA1c ≤7%), and Group 3 was the control group. Complete ophthalmic examination and OCT measurements were conducted to determine the thickness of the retina and choroidal tissue.* ***Results:*** *The mean central foveal thickness and the mean subfoveal CT were both statistically significant across all study groups. The mean HbA1c and subfoveal CT in all groups exhibited a statistically significant negative correlation; diabetics exhibited a thinner thickness than the control group. HbA1c and central macular thickness did not result in any significant correlations.* ***Conclusion:*** *Significant choroidal thinning is observed in diabetic patients, particularly those in the uncontrolled group (group 1). Additional research with a larger sample size is necessary to establish the correlation between CRT and CT and HbA1c and to determine the optimal cutoff value of HbA1c that impacts the choroid.*

Keywords: *Diabetes, Swept source OCT, Retinal thickness, Choroidal thickness, HbA1c*

1. Introduction

Diabetic retinopathy (DR) is the leading cause of blindness in people of working age and a common cause of visual impairment. However, it develops gradually over years and only manifests symptoms in its later stages [1]. The risk of sight-threatening consequences can be reduced if the lesions are detected before irreversible injury to retinal function has developed [2]. Objective quantification of macular thickness and quantitative monitoring of DME progression are feasible with the use of SS-OCT [2]. Moreover, DM can result in a number of patholo-

gical alterations in the choroid, including nonperfused regions, focal vascular dilatation, microaneurysms, and increased tortuosity [3]. Spectral domain optic coherence tomography has been employed in research to examine changes in choroidal thickness in DR [4]. The primary objective of glycated hemoglobin (HbA1c) measurement is to determine the average plasma glucose concentration over extended periods and to reflect the long-term management of hyperglycemia. In the Wisconsin Epidemiology Study of Diabetics, the incidence of DME is increased over a 10-year period by higher levels of HbA1c [5]. The World Health Organization has approved the usage of HbA1c for the diagnosis of DM, as evidenced by a number of epidemiological studies that indicate a threshold for an increased prevalence of microvascular complications at a HbA1c level of 6.5% [6].

2. Patients & Methods

This Comparative, non-interventional cross-section study performed at both SOAAD KAFAFI ophthalmology department, SOAAD KAFAI Hospital, Cairo, Egypt, and ASSUIT University, ASSUIT, EGYPT. Enrolled 90 eyes of divided into 3 groups. Group 1 included (30 eyes) of diabetic patients with poor glycemic control (HbA1c >7%) Group 2 included (30 eyes) of diabetic patients with good glycemic control (HbA1c ≤7%). Group 3 included (30 eyes) of age-matched non-diabetic candidates All groups undergone HbA1c level testing and OCT measurements for both retina and choroid at two centers in Egypt. Between October 2022 and was completed on 1st October 2023. Complete ophthalmic examination (BCVA, IOP, Ant segment, fundus examination), HbA1c and Oct measurements for both retinal (central 1 mm ETDRS thickness map) and choroidal thickness were performed. OCT images was captured by swept source OCT (DRI Triton, Topcon, Tokyo, Japan) after adequate dilation by Alcon Mydriacyl® eye drops (Tropicamide 1.0%). Choroidal thickness was measured by two methods: the first method by central sub foveal 1 mm ETDRS thickness map and the second method manually using a caliper. The mean thickness of retina and choroid in group 1 and 2 were compared to control group measurements.

2.1. *The inclusion criteria*

The inclusion criteria were Type 2 diabetes mellitus, ages 40 to 60 years, no prior ocular treatment (treatment-naïve), visual acuity of 0.1 LogMAR or better, capability to undergo an eye examination, spherical equivalent greater than ± 6 diopters (D), and axial length (AL) less than 26 mm. The exclusion criteria included amblyopia, glaucoma, vitreous-macular illnesses (such as vitreous hemorrhage and retinal detachment), diabetic retinopathy, a history of any major systemic diseases aside from diabetes, and any prior ocular surgeries or laser treatments. Subpar quality of fundus or OCT pictures due to aberrant refractive media (e.g., moderate to severe cataract, corneal ulcer, or severe pterygium), with OCT imaging quality ≤50, or inadequate fixation.

2.2. *Ethical consideration*

This comparative, non-interventional cross-sectional study was conducted in line with the Declaration of Helsinki. Informed written consent was collected from all study participants. The Ethics Committee of the Faculty of Medicine at Assiut Univ. examined and approved the study. Appropriate measures were implemented to ensure the privacy of participants and the confidentiality of the data as follows: We have anonymized the patients' identities in the research by assigning a code number

to each patient's name and address, which will be stored in a secure file. We have utilized the study's results just for scientific purposes and have not employed them for any other objectives.

2.3. *Statistical Analysis*

Statistical analysis was conducted using SPSS version 26 (IBM Inc., Armonk, NY, USA). An unpaired Student's t-test was used to compare the two groups' quantitative data, which were expressed as mean and standard deviation (SD). Qualitative variables were expressed as frequency and percentage (%) and evaluated using the Chi-square test or Fisher's exact test as applicable. A two-tailed P value of less than 0.05 was deemed statistically significant. The Pearson correlation was conducted to assess the extent of correlation between two quantitative variables.

3. Results

A total of 90 eyes of 49 participants that were classified into groups undergoing OCT measurements for both retinal and choroidal thickness and for HbA1c measurement were included. In group 1, uncontrolled diabetics, the mean age was 53.63 ± 7.41 years with range of 35-65 years. There was 7(43%) male and 9 (56.3%) females. In group 2, controlled diabetics, the mean age was 50.88± 9.02 years with range of 33-65 years. There was 7(43%) male and 9(56.3%) females. In group 3, Healthy controls, the mean age was 51.77± 9.19 years with range of 34.00-65.00 years. There was 7(43%) male and 10 (58.8%) females. There was no significant difference among the studied groups as regard age and sex, tab. (1). The mean duration of DM in group1 was 9.52 ±6.42 years with range of 1-20 years. While in group2 (controlled DM), the mean duration of DM was 8.31±5.85 years with range of 1-20 years. There is no significant correlation between duration of diabetes and both central retinal thickness and sub foveal choroidal thickness in both group 1 and 2, tab. (2)

Table 1: Comparison between three groups in Age & Sex:-

		Uncontrolled DM		Controlled DM		Healthy controls		F*	P value
		Mean	SD	Mean	SD	Mean	SD		
Age		53.63	7.41	50.88	9.02	51.77	9.19	0.40	**0.672 NS**
		N	%	N	%	N	%	X^{2**}	**P value**
Gender	***Male***	7	43.8%	7	43.8%	7	41.2%	0.03	**0.99 NS**
	Female	9	56.3%	9	56.3%	10	58.8%		

**One Way ANOVA test **Chi square test*

Table 2: Correlation between duration of diabetes (years) and thickness of both retina and choroid (all diabetic patients):

		Duration of diabetes (years)
Central retinal thickness	Pearson Correlation	0.09
	P value	0.64 NS
Sub foveal choroidal thickness	Pearson Correlation	-0.20
	P value	0.28 NS
Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI)	Pearson Correlation	-0.19
	P value	0.30 S

3.1. *Retinal and choroidal thickness*

A comparison between two methods of measuring choroidal thickness was done and there was no significant difference between two methods as shown in tab. (3).

After doing analysis of the results of both retinal and choroidal thickness it was found that in group 1, The mean Central retinal thickness was 247.87± 28.14 with range of 204.00-315.00. The mean Sub foveal choroidal thickness was 219.90± 52.80 with range of 89.00-340.00. The mean Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI) was 212.33± 51.11 with range of 100.00 - 333.00, tab. (4). In group 2, The mean Central retinal thickness was 248.87± 30.89 with range of 206.00-347.00. The mean Sub foveal choroidal thickness was 239.37± 81.07 with a range of 82.00-364.00. The mean Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI) was 242.17± 81.25 with range of 96.00- 350.00, tab. (4). In group 3, The mean central retinal thickness was 232.47± 24.67 with range of 191.00-277.00. The mean Sub foveal choroidal thickness was 280.33± 59.87 with range of 188.00-395.00. The mean Central 1 mm sub foveal choroidal, tab. (4). There was significant difference among the studied groups as regard Central retinal thickness, Sub foveal choroidal thickness and central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI), tab. (4). Central retinal thickness was significantly higher in uncontrolled DM and Controlled DM compared to Healthy controls with no significant between uncontrolled DM and Controlled DM. Sub foveal choroidal thickness was significantly lower in uncontrolled DM and Controlled DM compared to Healthy controls with no significant between uncontrolled DM and Controlled DM. Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI)was significantly lower in uncontrolled DM compared to Healthy controls with no significant between uncontrolled DM and Controlled DM with no significant between uncontrolled DM and Controlled DM and between Controlled Dm and Healthy controls, tab. (4).

Table 3: Comparison between two methods of measuring choroidal thickness

	Mean	SD	Mean difference	SD for difference	95% CI for difference	t*	P value
Sub foveal choroidal thickness(manual)	246.53	69.71	2.32	17	(-1.40) - (6.05)	1.24	0.22 NS
ETDRS thickness map BM-CSI	244.21	70.27					
***Paired samples t test**							

Table 4) Comparison of both Retinal and choroidal thickness in all study groups.

	Uncontrolled DM		Controlled DM		Healthy controls		F*	P value
	Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*		
Central retinal thickness	247.87	28.14	248.87	30.89	232.47	24.67	3.23	**0.04 S**
Sub foveal choroidal thickness (manual)	219.90	52.80	239.37	81.07	280.33	59.87	6.62	**0.002 HS**
central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI)	212.33	51.11	242.17	81.25	278.13	60.78	7.57	**0.001 HS**
***One Way ANOVA test**								

3.2. *Comparison of HBA1c in all study groups*

The mean HBA1c in group 1 was 9.78 ± 1.96 with range of 7.40-13.5. The mean HBA1c in group 2 was 6.33±.51 with range of 5.60-7.00. The mean HBA1c in group 3 was 5.01 ±.32 with a range of 4.50-5.70, tab. (5). *After doing correlation between HbA1c in different study groups.* In group1(uncontrolled DM), there was an insignificant correlation between HBA1c and Central retinal thickness, Sub foveal choroidal thickness and Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI), tab. (6). In group 2 (controlled DM), There was an insignificant correlation between HBA1c and Central retinal thickness, Sub foveal choroidal thickness and Central 1 mm sub foveal choroidal thickness (ETDRS

thickness map BM-CSI), tab. (6). In group 3 (healthy group), there was an insignificant correlation between Central retinal thickness and Sub foveal choroidal thickness, and Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI), tab. (6). *After a correlation was made between the three groups*. There was no statistically significant correlation between HBA1c and Central retinal thickness. There was a significant negative correlation between HBA1c and Sub foveal choroidal thickness, Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI), tab. (7).

Table 5: Comparison of HBA1c in all study groups

Groups		Min.	Max.	Mean	SD
1(uncontrolled DM)	HBA1c	7.40	13.50	9.78	**1.96**
2(controlled DM)	HBA1c	5.60	7.00	6.33	**0.51**
3(Healthy)	HBA1c	4.50	5.70	5.01	**0.32**

Table 6: Correlation between HBA1c level and thickness of both retina and choroid in each group

Group1		HBA1c
Central retinal thickness	Pearson Correlation	-0.02
	P value	0.91 NS
Sub foveal choroidal thickness(manual)	Pearson Correlation	-0.07
	P value	0.71 NS
Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI)	Pearson Correlation	0.01
	P value	0.97 NS
Group 2		
Central retinal thickness	Pearson Correlation	0.20
	P value	0.30 NS
Sub foveal choroidal thickness	Pearson Correlation	0.05
	P value	0.79 NS
Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI)	Pearson Correlation	0.08
	P value	0.68 NS
Group3		
Central retinal thickness	Pearson Correlation	0.17
	P value	0.38 NS
Sub foveal choroidal thickness(manual)	Pearson Correlation	0.08
	P value	0.68 NS
Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI)	Pearson Correlation	-0.10
	P value	0.59 NS

Table 7: Correlation between HBA1c level and thickness of both retina and choroid (among all study participants)

		HBA1c
Central retinal thickness	Pearson Correlation	0.17
	P value	0.11 NS
Sub foveal choroidal thickness(manual)	Pearson Correlation	-0.30
	P value	0.01 HS
Central 1 mm sub foveal choroidal thickness (ETDRS thickness map BM-CSI)	Pearson Correlation	-0.31
	P value	0.003 HS

4. Discussion

Efficient control of glycemic status and BP are considered the most important modifiable risk factors to decrease the risk of progression of DR and vision loss among several associated risk factors in diabetic patients [7]. In our study, there was a statistically significant difference regarding central foveal thickness between all study groups which was higher among diabetic patients regardless their diabetic control. Qing Zhao et al. [8], Nagaoka et al. [9], Torabi et al. [10] and Fernández-Espinosa

et al [7]. Also supported this finding. While regarding sub foveal choroidal thickness, it was thinner in diabetic groups more than control group, with a statistically significant difference. Our results are comparable with many other studies done by Kim et al. [11], Esmaeelpour, et al. [12], Sudhalkar, et al. [13], Lee, et al. [14] and Yolcu U. et al. [15]; which demonstrated that choroidal hypoxia and ischemia are caused by variations in the choriocapillaris and a decrease in choroidal blood flow that occur in diabetic individuals, and as a consequence choroidal thinning. On the other hand, Torabi and his coworkers, found that the choroidal thickness in non-diabetic patients was significantly greater than in diabetic patients. this may be due to that our study included diabetic patients with longer duration of diabetes than diabetic patients in their study [10]. while Lee and his co-workers found that there is no discernible difference between the normal control eyes and the diabetic eyes without DR [14]. Hemoglobin A1c (HbA1c) is one of the standard tools to assess glycemic control and its optimum value is 5.6–7% in patients with diabetes [16]. In our study, there was lack of significance with positive correlation between HbA1c and central macular thickness suggests that, even longer-term measures of diabetes such as disease duration, may be necessary to understand changes in retinal architecture. while Asefzadeh, et al. [17] and Srinivasan, et al. [18] support this result, Sharma et al., found a statistically significant positive correlation between CRT and HbA1c. This may be related to the included patients had diabetic retinal changes [19] while in our study diabetic retinopathy changes was an exclusion criteria. The negative correlation between HbA1c and sub foveal CT which was statistically significant was comparable with the studies obtained by Kase et al. [20] and, Unsal et al. [21]. Thus, it is anticipated that the choroid will be thinner in patients with uncontrolled diabetes mellitus and elevated HbA1c. On the other hand, Fernández-Espinosa et al. highlighted that there was no significant correlation found [7]. And that can be explained by, the time evolution of DM of the enrolled diabetic patients in his study was shorter than ours, so according to his study CT has no correlation in the beginning of the disease [7]. Diabetes is a key condition that notably influences choroidal thickness. Consequently, stringent diabetes management and regular HbA1c assessments every three months may avert choroidal vascular impairment and choroidal atrophy, thereby preventing central retinal edema and the progression of diabetic retinopathy (DR). Future research with bigger sample sizes are necessary to ascertain the relationship between CRT and CT with HbA1c and to identify the ideal HbA1c cutoff value that influences the choroidal vascular system.

5. Conclusion

Regardless of diabetic control, we found that the central foveal thickness was greater in diabetic patients than in the control group (non-diabetic group). And when HbA1c levels rise, CRT rises as well. In contrast, diabetes patients with moderate or poor glycemic control (HbA1c > 7%) had thinner choroidal thickness, while normal control subjects had choroidal thickness that was nearly equivalent to that of diabetic patients with good glycemic control. As a result, strict diabetes management and regular Hba1c testing every three months may stop choroidal vascular damage and thinning, which in turn may stop central retinal edema and the onset of DR. Future research with a bigger sample size is necessary to establish the relationship between HbA1c and CRT and CT, as well as to identify the ideal HbA1c cutoff value that influences the choroidal vascular system.

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