

Assessment of Macular and Choroidal Thickness in Diabetic Patients in Relation to Glycemic Control

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Abstract

Background: Retinopathy, or diabetic eye disease, is a condition in which damage to the retina develops as a result of diabetes. One potential consequence of DR is blindness.

Aim and objectives: The purpose of assessing diabetes patients' glucose control in relation to choroidal and macular thickness is to.

Subjects and methods: Patients with diabetes who visited the Retina clinic at Al-Azhar University Hospitals between January 2024 and October 2024 were the subjects of this non-cohort, cross-sectional study. Patients were subdivided according to HbA1c levels into 3 subgroups: group-A HbA1c 7 and below, group-B 7-8% and group-C HbA1c above 8%. Each group was examined for SF CT and CMT by OCT.

Results: The groups varied significantly in terms of sub-foveal choroidal thickness (μm). Group A had the highest mean value (289.47 ± 49.7), followed by group B (219.6 ± 30.9), and group C had the lowest value (192.46 ± 20.6). Based on central macular thickness (CMT), there is an extremely significant difference between the groups. Group-C had the highest mean value (283.98 ± 50.96), followed by group-B (250.99 ± 41.3), and group-A had the lowest (216.8 ± 29.6).

Conclusion: From the results of this study we concluded that, there were positive correlation between HbA1c levels with CMT and negative with SF CT.

Keywords: Glycemic Control; Choroidal Thickness; Macular Thickness; DM

1. Introduction

The integrity of the retina's tiny vessels is primarily affected by diabetic retinopathy (DR), a degenerative condition. PDR, or proliferative diabetic retinopathy, and NPDR, or non-proliferative diabetic retinopathy, are the two main clinical stages of DR.¹

Dot and blot hemorrhages are the end result of microaneurysms that occur in NPDR as a consequence of hyperglycemia's damage to the capillary walls. Additionally, retinal edema is caused by the weaker arteries becoming leaky. Hard exudates, a yellow precipitate of lipid leftovers, can be left behind as fluid resolves. A condition known as cotton wool spots (CWS)

can develop as NPDR advances due to the blockage of afflicted vessels, which can lead to infarction of the nerve fiber layer.²

Macular edema is the leading cause of blindness in diabetics, although neovascularization in PDR can have catastrophic consequences. Although macular edema can develop in non-percutaneous DR (NPDR), it is more frequently seen in advanced DR instances when the new blood vessels are permeable.³

Half of all people with PDR will go blind within five years of diagnosis if therapy is not started. Thanks to optical coherence tomography (OCT), we may now objectively evaluate macular thickness and statistically track the evolution of DR.⁴

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Periodic measures of glycosylated hemoglobin (HbA1c) can be used to monitor the long-term control of hyperglycemia. Clinical investigations examining the prevention, management, and consequences of diabetes have demonstrated that strict adherence to maintaining a steady blood sugar level considerably decreases the incidence of diabetic retinopathy in individuals with type 1 and type 2 diabetes.⁵

This research set out to examine diabetic individuals' choroidal and macular thickness in connection to their ability to maintain stable blood sugar levels.

2. Patients and methods

Patients with diabetes who visited the Retina clinic at Al-Azhar University Hospitals between January 2024 and October 2024 were the subjects of this case series descriptive study.

Ethical approval:

The research was approved by Medical Research Ethics Committee at Al-Azhar University. Participation in the trial was contingent upon each patient signing an informed written consent form.

Inclusion criteria:

Individuals with type 2 diabetes.

Exclusion criteria:

People who have a history of type 1 diabetes mellitus in their family, a history of glaucoma, high myopia, optic nerve pathology, vitreous hemorrhage, dense cataract, hypertension, systemic medications (to rule out the possibility of their impact on macular thickness), and a history of ocular surgeries (such as retinal procedures or prior laser treatments) should not undergo cataract surgery.

Methodology:

Patients with type II diabetes mellitus were divided into three groups in this prospective case series according to their HbA1c levels:

Group-1 included 30 eyes from patients with good glycemic control (HbA1c $\leq$ 7%), Group-2 included 30 eyes from patients with intermediate glycemic control (HbA1c within 7% and 8%), and Group-3 included 30 eyes from patients with poor glycemic control (HbA1c $\geq$ 8%).

All patients were subjected to:

Thorough medical history review, meticulous eye exam on the day of OCT evaluation, measurement of intraocular pressure using a Goldman applanation tonometer, examination of the anterior and posterior segments using slit-lamp biomicroscopy, and examination of the dilated fundus using both slit-lamp biomicroscopy with a 90D lens and indirect ophthalmoscopy were all part of the process.

Investigations:

HbA1c level assessment:

When the OCT evaluation was to take place, a blood sample was drawn to determine the HbA1c level. The laboratory at Al-Azhar University Hospital used the COBAS INTEGRA 400 plus to measure the HbA1c level.

Axial length measurement:

The axial lengths were determined by Topcon ALADDIN HW 2.0 at the Ophthalmology department, Al-Azhar University Hospital.

Macular & choroidal thickness measurement:

An eye doctor from Tokyo, Japan, named Topcon, used a DRI-1 Swept Source SS OCT to assess the thickness of the choroidal and macular retinas. When it comes to imaging the eye's posterior segment, it's the first swept source OCT ever created. A light source with an 840 nm wavelength. They used a resolution of 6 μ m and a scanning speed of 27,000 A scans/second, which is twice as fast as spectral domain (SD) OCT. Thanks to these features, swept source optical coherence tomography (SSCT) scans were more sensitive and better able to distinguish between the vitreous and choroid.

Macular thickness measurement:

Before scanning, patients were given tropicamide eye drops 1.0% to pharmacologically dilate their pupils; this was repeated three times every five minutes. They were then advised to concentrate on an internal fixation target. An external fixation target was used to move the scanning region centrally over the macula when fixation was not central. The 3D-macula method was used to measure macular thickness. To get precise thickness readings, we imaged the thinnest area of the macula, which meant taking scans very close to the fovea. In this approach, we could eradicate any errors brought forth by minute differences in location.

Automatic segmentation of OCT images was performed using the segmentation algorithms integrated within the Topcon 3D-OCT 2010 software in order to generate the retinal thickness map. These algorithms define the retinal pigment epithelium (RPE) and internal limiting membrane (ILM). A grid of automatically registered ETDRS points was superimposed on top of the topographical map for each eye. It is necessary to manually reposition the ETDRS grid if it was not properly positioned over the fovea. By moving the mouse pointer over the retinal thickness map in the macular region, we were able to calculate the maximum retinal thickness (MRT). When the quality factor fell below 40, no scans were considered.

The 3D macula procedure used a raster-scan of 512 $\times$ 256 axial scans to quantify macular thickness over an area of 7 $\times$ 7mm in the macular region. Reconstructing a color topographic image with numerical averages of thickness data for each of

the nine map parts was done using the ETDRS-defined 7×7mm area centered on the fovea. The ETDRS map revealed nine distinct regions within the macula, all of which were concentrated on the fovea. A diameter of 1 mm was found in the innermost area, 3 mm in the middle area, and 6 mm in the outermost area. The 3 mm inner ring and 6 mm outer ring are divided into four equal pieces; the fovea is located in the innermost 1 mm ring. Measurements of the inner limiting membrane (ILM) to the inner boundary of retinal pigment epithelium allowed for the identification of retinal layers and the measurement of macular thickness.

Focal thickness was defined as macular thickness inside the innermost 1-mm ring. In order to determine the mean macular thickness (AMT), the nine regions of the ETDRS map were averaged. Glycated hemoglobin was shown to be correlated with only two variables—average macular thickness (AMT) and foveal thickness (CMTH)—out of all nine ETDRS regions.

Choroidal thickness measurement:

The distance known as CT was used to describe the angle between the choroid/sclera junction and the posterior edge of the hyper-reflective RPE. The built-in mapping software was used to automatically compute the choroidal thickness and present it as a topographic map. The map was divided into nine subfields defined by an ETDRS-style grid. The following stage involved making a three-dimensional topographical map of thicknesses.

The neural circuit topology (SFCT) in the inner ring, temporal inner macula, nasal outer macula, superior outer macula, temporal outer macula, and inferior outer macula were the nine ETDRS subfields that were automatically computed. Bands of 1,3, and 6 mm in diameter encircled the periphery maculas.

The choroidal borders were segmented using the built segmentation modification tool. The twelve radial scans were automatically produced using the choroidal-scleral boundary and the retinal pigment epithelium (RPE) as reference lines. The next step was a manual check of each line for misalignment and correction, if needed.

Exactly one out of the nine regions that make up the ETDRS, the subfoveal choroidal thickness, the choroidal thickness at the temporal point (which is located at a distance of 1500um from the foveal center), and the choroidal thickness at the nasal point (also located at a distance of 1500um from the foveal center) were selected for correlation with glycated hemoglobin.

Statistical analysis:

Data were analyzed using SPSS Inc.'s social science statistical software, version 23.0. We gave quantitative values as ranges and mean±standard deviation. Qualitative features were represented

by numbers and percentages.

We used Tukey's test for multiple variable comparisons and a one-way ANOVA for more than two means. A post-hoc test was also done. We utilized Fisher's exact test instead of Chi-square test to compare qualitative groups when any cell had an anticipated count of less than 5.

Both a 95% confidence interval and 5% error margin were allowed. This is why the p-value was significant: Expectations Significant results were less than 0.05, very significant were less than 0.001, and insignificant were larger than 0.05.

3. Results

Table 1. Comparison between groups according to demographic data.

DEMOGRAPHIC DATA	GROUP-A (N=15)	GROUP-B (N=15)	GROUP-C (N=15)	TEST VALUE	P-VALUE
AGE				2.31	0.479
MEAN±SD	51.07±10.37	49.32±11.2	50.57±9.96		
RANGE	44-60	45-63	46-62		
GENDER				1.32	0.641
MALE	7(46.7%)	6(40%)	6(40%)		
FEMALE	8(53.3%)	9(60%)	9(60%)		
EYES				1.49	0.415
OD	15(50%)	15(50%)	15(50%)		
OS	15(50%)	15(50%)	15(50%)		

Statistical analysis of gender, age, and eye-related demographic data reveals no discernible difference between the categories (p-value) (p>0.05).

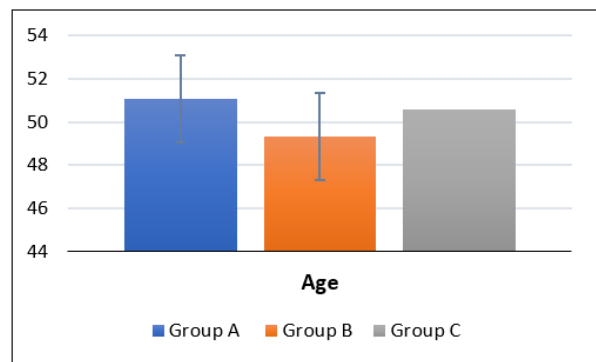


Figure 1. Group comparisons based on age.

Table 2. Group comparison based on illness duration (in years).

VARIABLES	GROUP-A (N=15)	GROUP-B (N=15)	GROUP-C (N=15)	TEST -VALUE	P-VALUE
DISEASE DURATION (YEARS)				6.97	0.001*
MEAN±SD	4.22±3.1	6.34±3.6	8.11±4.32		
RANGE	1-5	2-15	1.5-18		

This table shows statistically significant higher mean value in group-C, followed by group-B and the lowest value in group-A, with p-value(p=0.002)

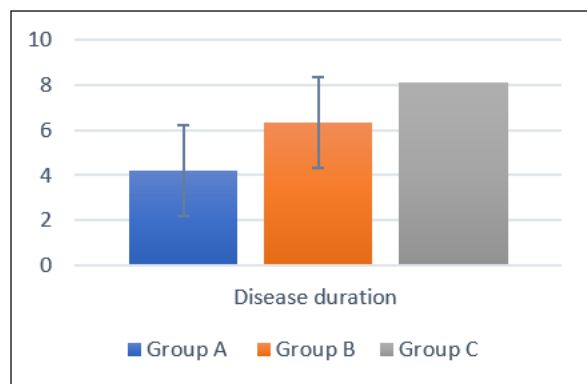


Figure 2. Analysis of groups based on illness duration.

Table 3. Evaluation of subgroups based on macula thickness.

VARIABLES	GROUP-A (N=15)	GROUP-B (N=15)	GROUP-C (N=15)	TEST-VALUE	P-VALUE
CENTRAL MACULAR THICKNESS(UM)				7.95	0.001*
MEAN±SD	216.8±29.6	250.99±41.3	283.98±50.96		
RANGE	164-318	172-297	202-308		
AVERAGE MACULAR THICKNESS(UM)				8.62	0.001*
MEAN±SD	242.96±12.9	261.96±25.41	277±13.5		
RANGE	241.3-283.2	171.3-291.9	171.3-297.7		

Based on the central macular thickness, the table reveals that group-A has the lowest value, followed by group-B, and group-C has a significantly greater mean value ($p<0.001$). A statistically significant difference was found between groups A and B using Tukey's post hoc test, although group C had the highest mean value, followed by group B, and group A had the lowest value in terms of average macular thickness ($p<0.001$).

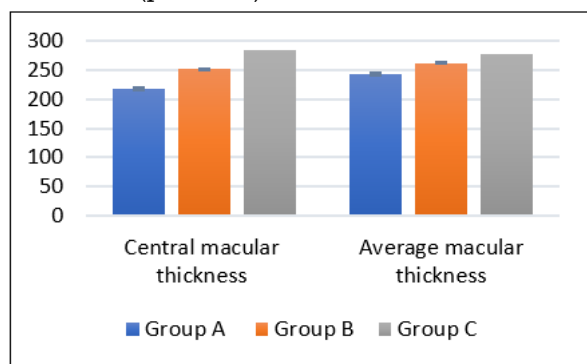


Figure 3. Evaluation of subgroups based on macula thickness.

Table 4. Evaluation of categories based on choroidal thickness.

VARIABLES	GROUP-A (N=15)	GROUP-B (N=15)	GROUP-C (N=15)	TEST-VALUE	P-VALUE
SUB FOVEAL CHOROIDAL THICKNESS(UM)				7.32	0.001*
MEAN±SD	289.47±49.7	219.6±30.9	192.46±20.6		
RANGE	144-366	95-337	110-337		
CHOROIDAL THICKNESS AT NASAL POINT(UM)				8.32	0.001*
MEAN±SD	221.4±48.6	176.3±37.96	164.9±30.96		
RANGE	109-300	87-324	80-324		
CHOROIDAL THICKNESS AT TEMPORAL POINT(UM)				9.35	0.001*
MEAN±SD	265.9±61.7	211.9±41.3	191.7±29.79		
RANGE	110-376	108-360	88-360		

According to sub foveal choroidal thickness,

group-A has a significantly larger mean value than group-B and group-C has the lowest value. However, Tukey's post hoc test did not find a significant difference between groups-B and C.

Group C had the lowest choroidal thickness at the nasal point (um), while groups A and B had significantly greater means ($p=0.007$). However, Tukey's post hoc test did not find a significant difference between groups C and B.

Group C had the lowest choroidal thickness at the temporal point (um), followed by group A with a highly significant higher mean value ($p<0.001$), although Tukey's post hoc test did not find a significant difference between groups B and C.

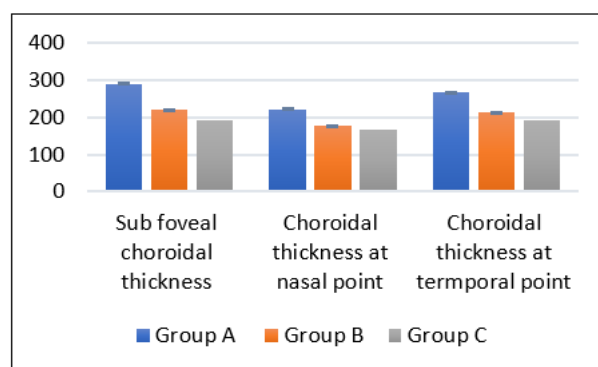


Figure 4. Comparison between groups according to choroidal thickness.

Table 5. Analysis of the Pearson Correlation Coefficient to determine the relationship between choroidal and macular thickness in all cases

	AGE (YEARS)	DISEASE DURATION (YR)	HBA1C LEVEL	IOP	SPHERICAL EQUIVALENT	AXIAL LENGTH (MM)
ALL STUDIED						
CASES						
CENTRAL MACULAR THICKNESS (UM)	r-value 0.626 P-value 0.035*	r-value 0.693 P-value 0.001*	r-value 0.846 P-value 0.001*	r-value -0.616 P-value 0.047*	r-value 0.411 P-value 0.453	r-value -0.641 P-value 0.037*
AVERAGE MACULAR THICKNESS (UM)	r-value 0.322 P-value 0.443	r-value 0.68 P-value 0.001*	r-value 0.913 P-value 0.001*	r-value -0.255 P-value 0.45*	r-value 0.453 P-value 0.456	r-value -0.346 P-value 0.32
SUB FOVEAL CHOROIDAL THICKNESS (UM)	r-value 0.285 P-value 0.34	r-value -0.383 P-value 0.001*	r-value -0.485 P-value 0.001*	r-value 0.404 P-value 0.41	r-value 0.531 P-value 0.279	r-value -0.451 P-value 0.023*
CHOROIDAL THICKNESS AT NASAL POINT (UM)	r-value 0.428 P-value 0.574	r-value -0.52 P-value 0.001*	r-value -0.936 P-value 0.001*	r-value 0.348 P-value 0.366	r-value 0.342 P-value 0.393	r-value -0.548 P-value 0.021*
CHOROIDAL THICKNESS AT TEMPORAL POINT (UM)	r-value 0.219 P-value 0.392	r-value -0.728 P-value 0.001*	r-value -0.782 P-value 0.001*	r-value 0.543 P-value 0.54	r-value 0.413 P-value 0.542	r-value -0.299 P-value 0.034*

An association between age in years and central macular thickness was found to be statistically significant ($p<0.05$). Similarly, when looking at the duration of the disease, there was a positive correlation between central macular thickness and average macular thickness ($p<0.05$). On the other hand, there was a negative correlation with sub foveal choroidal thickness (um), choroidal thickness at the nasal point and temporal point (um), as well as

thickness (um), choroidal thickness at the nasal point and temporal point (um), and an association with thickness (um), thickness (um), and choroidal thickness at the temporal point (um) ($p < 0.05$); Regarding the HbA1c level, a positive correlation was found with both central macular thickness and average macular thickness at a p-value of less than 0.05. Additionally, there was a negative correlation between the HbA1c level and sub foveal choroidal thickness, choroidal thickness at the nasal point, and choroidal thickness at the temporal point, with a p-value of less than 0.001. The intraocular pressure (IOP) showed a significant positive correlation with average macular thickness at a p-value of less than 0.05. Axial length (mm) had a statistically significant negative correlation with central macular thickness at a p-value less than 0.05. Finally, sub foveal choroidal thickness, choroidal thickness at the nasal point, and choroidal thickness at the temporal point were all.

Case Presentation:

case 1:(group-B)

Male patient 56-years old, HbA1c:7.8%, disease duration:8-years.

ITEM	RIGHT-EYE	LEFT-EYE
CMT(μM)	245	252
AMT(μM)	262.3	267.1
SUB FOVEAL CHORIDAL THICKNESS(μM)	206	224

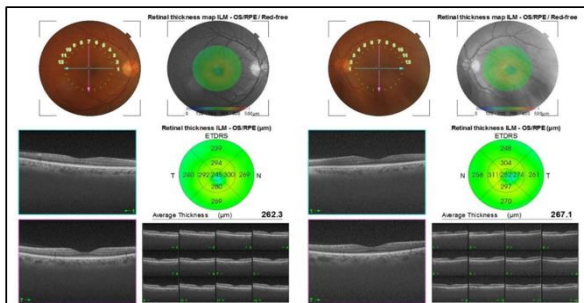


Figure 5. OCT printout showing macular thickness of a case in group-B.

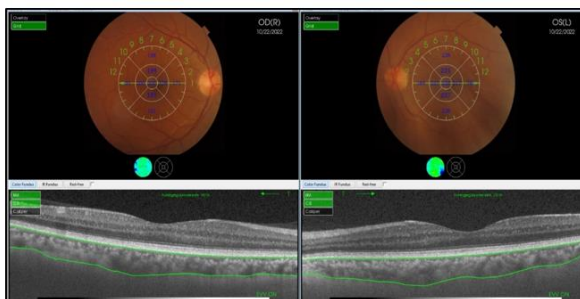


Figure 6. OCT printout showing choroidal thickness measurements of a case in group-B.

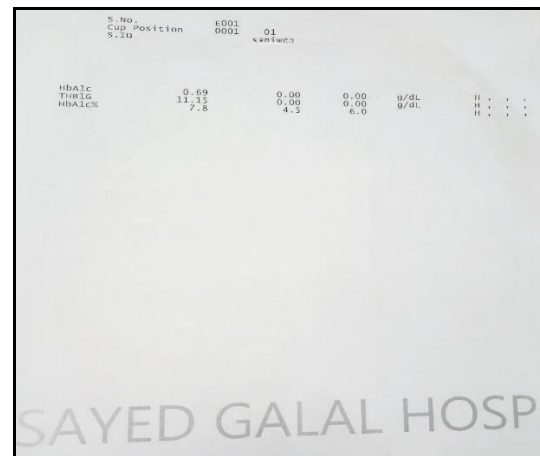


Figure 7. HbA1c printout of a case in group-B.

case 2:(group-C)

Female patient 58-years old, HbA1c:8.8%, disease duration:11-years.

ITEM	RIGHT-EYE	LEFT-EYE
CMT(μM)	274	285
AMT(μM)	278	291.9
SUB FOVEAL CHORIDAL THICKNESS(μM)	110	150

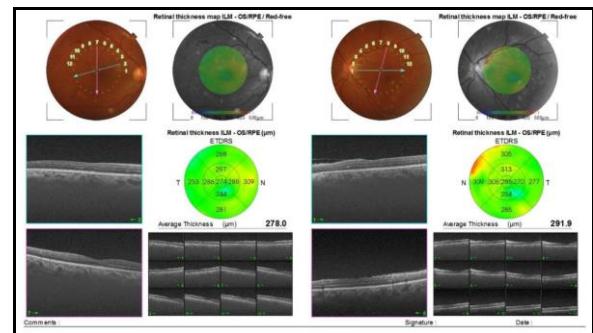


Figure 8. OCT printout showing macular thickness measurements of a case in group-C.

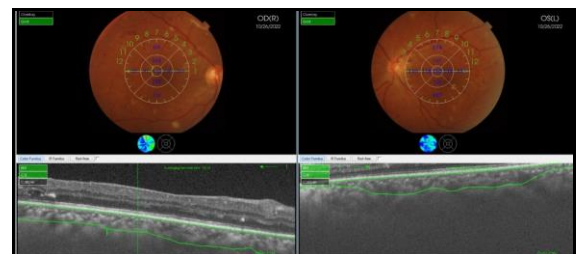
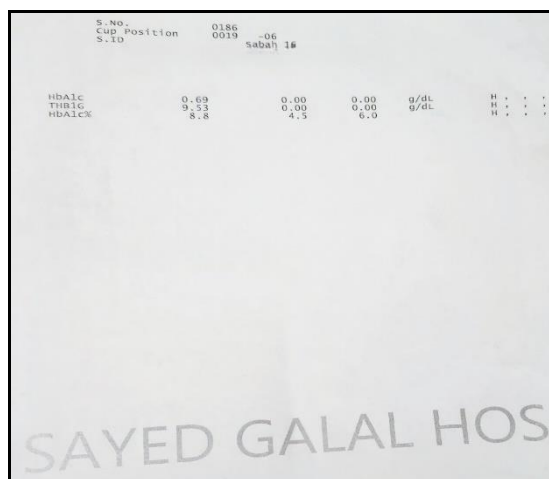


Figure 9. OCT printout showing choroidal thickness measurements of a case in group-C.



S.No.	0186	06			
Cup Position	0019	06			
S-10	0019	06			
HbA1c	0.69	0.00	0.00	g/dL	H + + +
TIRIC	9.53	0.00	0.00	g/dL	H + + +
HbA1c	8.8	4.5	6.0		H + + +

Figure 10. HbA1c printout of a case in group-C.

4. Discussion

In this research, we showed that groups varied significantly in terms of central macular thickness (CMT), with group C having the highest mean value (283.98 ± 50.96), group B having the second highest (250.99 ± 41.3), and group A having the lowest (216.8 ± 29.6).

Additionally, when looking at average macular thickness (AMT), there is a notable disparity across the groups. Group-C had the highest mean value (277 ± 13.5), group-B had the second highest (261.96 ± 25.41), and group-A had the lowest (242.96 ± 12.9).

Statistical analysis revealed a favorable association between HbA1c level and both central and average macular thickness in the research groups.

Supporting our results, Demir et al.,⁶ observed no statistically significant increase in central macular thickness compared to healthy controls in individuals with type 2 diabetes mellitus who did not have clinical retinopathy.

Yeoung et al.,⁷ found that in individuals with type I and type II diabetes for 10 years or more without diabetic macular edema, there was a favorable correlation between HbA1c level and macular thickness. Evidence from this study points to the possibility of pre-clinical alterations in retinal volume and thickness prior to the clinical manifestation of diabetic macular edema (DMO).

Hamed et al.,⁸ discovered that the control HbA1c group had thinner macular thickness (MT) than the uncontrolled HbA1c group.

Benarous et al.,⁹ found that HbA1c levels varied across different eye conditions, with 7.3 for patients without DR, 8.0 for eyes with DR, 8.1 for eyes with DME, and 8.3 for eyes with CSME.

Jew et al.,¹⁰ discovered that HbA1c levels were considerably greater in the eyes affected by

CSME (10.38%) than in the eyes unaffected by CSME (7.8%). Among the important risk factors for developing CSME, they demonstrated that HbA1c values were.

Cetin et al.,¹¹ discovered that the HbA1c level was 8.6% higher in eyes affected by DME compared to eyes unaffected by DME (7.9%).

Romero Aroca et al.,¹² found that between the ages of 60 and 66, there was a correlation between macular edema, greater glycosylated hemoglobin levels, and more severe retinopathy.

Teberik et al.,¹³ discovered that controls had thinner mean CMTs than type 2 DM patients without diabetic retinopathy, however this difference did not reach statistical significance. There was no relationship discovered between CMT and HbA1c, fasting plasma glucose levels, or duration of DM.

Therefore, it is reasonable to assume that close monitoring of blood sugar levels is linked to a slower onset and worsening of diabetic retinopathy. The risk of diabetic macular edema (DME) rose when the hemoglobin A1c level was seven or higher. Another risk factor for developing DME is the duration of diabetes. However, because type II DM symptoms are vague and patients sometimes have trouble remembering them, reported durations of the disease are often unreliable. Some patients had known diabetic problems at the time of diagnosis, suggesting that they had probably been living with the condition for quite some time.

Group A had the highest mean value (289.47 ± 49.7), group B had the second-highest (219.6 ± 30.9), and group C had the lowest (192.46 ± 20.6), as demonstrated in this study, which compared groups based on sub-foveal choroidal thickness (μm).

Group-A had the highest mean value of choroidal thickness at the nasal point (221.4 ± 48.6), followed by group-B with a value of 176.3 ± 37.96 , and group-C with the lowest value of 164.9 ± 30.96 . This difference is statistically significant.

Group-A has the highest mean value (265.9 ± 61.7), followed by group-B (211.9 ± 41.3), and group-C has the lowest value (191.7 ± 29.79) when it comes to choroidal thickness at the temporal point (μm). This difference is extremely significant according to statistical analysis.

Statistical analysis revealed a negative connection between hemoglobin A1c and sub-foveal choroidal thickness, choroidal thickness at the nasal point, and choroidal thickness at the temporal point across all analysis groups.

Abadia et al.,¹⁴ in line with our research, assess the thickness of the choroidal tissue in the SF region as well as at five distinct locations along the nasal and temporal arteries using SS-OCT. The results showed that the sub-foveal, temporal,

and nasal choroidal regions were noticeably thinner in type 2 diabetic patients, moderate NPDR patients, and DME patients compared to healthy participants. The entire group found a small negative relationship between HbA1c and the thickness of the central choroids (both subfoveal and N1).

On the other hand, our research, Kim et al.,¹⁵ assessed the thickness of the choroidal and subfoveal layers at 1500µm above, below, nasally, and laterally to the fovea with the use of SD-OCT. They discovered that compared to eyes without DR or eyes with mild/moderate or severe NPDR, the sub-foveal choroidal thickness in PDR was thicker. They found that choroidal thickness expanded considerably from mild, moderate, and severe non-proliferative DR (NPDR) to proliferative DR (PDR) as the severity deteriorated. Eyes affected by DME have a thicker subfoveal choroid compared to eyes free of DM.

4. Conclusion

When it comes to diagnosing macular and choroidal thickness, optical coherence tomography is the way to go because it is both sensitive and noninvasive. Hemoglobin A1c levels have a positive correlation with central macular thickness (CMT) and average macular thickness (AMT) amongst the research groups, and a negative correlation with subfoveal choroidal thickness (SFCT), nasal point choroidal thickness (NT), and temporal point choroidal thickness (TFCT). A decrease in ischemia and effects on the onset and course of diabetic retinopathy may result from strict adherence to a glucose-lowering regimen that also affects the choroidal and retinal vasculature. The likelihood of developing macular edema and choroidal thinning increases when blood glucose levels reach seven or higher.

Disclosure

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All authors have a substantial contribution to the article

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