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Evaluation of the Choroid in Patients with Non Proliferative Diabetic Retinopathy by Optical Coherence Tomography Angiography (OCTA)

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CASE SERIES

Evaluation of the Choroid in Patients with Nonproliferative Diabetic Retinopathy by Optical Coherence Tomography Angiography

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Abstract

Background: **Diabetes may cause a wide range of eye disorders, including cataracts, glaucoma, other ocular abnormalities, recurrent styes, nonarteritic anterior ischemic optic neuropathy, and diabetic papillopathy.**

Objective: **Optical coherence tomography angiography was used to examine the capillaries of the retina in patients with diabetic retinopathy with nonproliferative disease.**

Patients and methods: **This was a prospective cross-section clinical study that was carried out on 60 eyes of 34 patients, who were divided into two groups: group A included 30 eyes of 19 patients with different stages of nonproliferative diabetic retinopathy (NPDR), and group B included 30 eyes of 15 healthy participants with normal healthy eyes as the control group. All participants were selected from patients attending the outpatient ophthalmology clinic of Memorial Institute of Ophthalmic Research between December 2020 and December 2021.**

Results: **As a result of the sugar profile, the duration of diabetes mellitus ranged from 8 to 25 years, with an average of 12 years. The fasting blood sugar and glycated hemoglobin values in the cases group were significantly higher than in the control group. Renal function and lipid profile did not vary significantly between patient and control groups. As far as eye examinations were concerned, there was no difference between the patients and controls regarding best-corrected visual acuity, uncorrected visual acuity, and intraocular pressure.**

Conclusion: **In the macular region, choriocapillaris (CC) flow areas are significantly reduced in patients with NPDR; moreover, CC blood flow is affected by glycated hemoglobin, suggesting that patients with NPDR and poor glycemic control may have significant impairment of CC blood flow.**

Keywords: Choroid, Nonproliferative diabetic retinopathy, Optical coherence tomography angiography

1. Introduction

As a result of the long-term effects of diabetes, diabetic retinopathy (DR) causes damage to and ultimately blinds the retina. For those who are in their prime working years in the western world, it is the most prevalent cause of significant vision loss.[1]

There are two different clinical stages of DR: nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR). Increased permeability and capillary obstruction are seen in the retinal vasculature at this stage. Fundus photography may identify early signs of retinal abnormalities such microaneurysms, hemorrhages, and hard edema.[2]

Neovascularization is a common occurrence in late stages of diabetes. A vitreous hemorrhage or tractional retinal detachment caused by newly formed aberrant arteries may occur at this moment, resulting in significant visual loss for the patient. Diabetic macular edema is the most prevalent cause of visual loss in patients with DR.[2]

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This causes the macula to become larger or thicker owing to a deficiency in the retinal blood–retinal barrier. At any point throughout the DR process, diabetic macular edema may arise and cause visual abnormalities as well as a reduction in visual acuity. Laser photocoagulation, intravitreal pharmaceutical medicines, and vitreous surgery are currently employed to address DR's microvascular issues.[3]

Poor glycemic control, high blood pressure, dyslipidemia, nephropathy, male sex, and obesity all contribute to retinopathy. To avoid DR-related blindness, early detection and timely treatment are also essential components.[4]

Optical coherence tomography (OCT) has been a game changer in the realm of ocular imaging. Optical coherence tomography angiography (OCTA) has expanded on this basis, delivering depth-resolved images beyond those obtained by prior imaging technologies.[5]

Ophthalmic capillary network and foveal avascular zone are noninvasively seen by OCTA. Using this method, high-resolution perfusion maps of the central retinal vasculature have also been made.[6]

The superficial capillary plexus (SCP), the deep capillary plexus (DCP), the outer retinal layer (ORL), and the choriocapillaris (CC) are all parts of the retina–choroid complex. An analysis of the percentage of sample area occupied by artery lumens was used to measure vascular density after binary image reconstruction. For example, DR may be detected and monitored with the use of this method.[7]

Study participants with NPDR underwent OCTA to examine the choroidal vasculature.

The aim was to use OCTA was to examine the capillaries of the retina in DR patients with nonproliferative disease.

2. Patients and methods

An ETDRS-based prospective cross-sectional clinical study involving 60 eyes from 34 participants was carried. The patients were divided into two groups: group A included 30 eyes from 19 patients with varying stages of NPDR, and group B included 30 eyes from 15 age-matched healthy participants with normal healthy eyes as controls. The ETDRS classification system was used in this study. Patients at the outpatient ophthalmology clinic were used as participants for this study.

The ethics committee of Al-Azhar University, Faculty of Medicine, Egypt, approved this study, which was carried out in accordance with the Declaration of Helsinki's guidelines for clinical research.

Inclusion criteria were as follows: those who had NPDR, both sexes, patients between the ages of 30 and 60 years, and patients with a normal anterior segment examination and suitably clear media who had diabetes for around 8 years.

Exclusion criteria were as follows: patients who were younger than 30 years or older than 60 years; anyone who wears contact lenses and had any media capacity that prevents a sufficient clinical assessment; patients with PDR; patients with additional vascular or metabolic problems; individuals with a prior history of intravitreal injections of steroids or anti-vascular endothelial growth factor; patients who previously had panretinal photocoagulation or focused, grid laser application; those who have either inherited or acquired macular dystrophic disease; patients having a history of retinal detachment, ocular inflammation, or ocular surgery; and patients with any of these conditions.

All study participants were subjected to the following.

2.1. Complete history taking

It included the following:

Personal history such as name, age, and sex.

Ocular history such as previous history of ocular surgeries; trauma; onset, course, and duration of diabetes mellitus (DM); measurement of spherical refractive error; and if there was any other ocular complaint.

Medical history of insulin, oral hypoglycemic drugs, systemic and topical ocular medication, or laser application.

Past history and family history of any chronic metabolic, vascular, renal, cardiac, or pulmonary diseases or history of similar condition.

2.2. Clinical examination

It included the following

General examination to exclude any systemic conditions that might affect ocular blood flow such as hypertension, systemic lupus erythematosus, anemia, or cardiovascular disease.

Full ophthalmic examination: a slit-lamp biomicroscopy or a binocular indirect ophthalmoscope may be used to rule out any abnormalities or ocular surface disease. To measure both best-corrected visual acuity and uncorrected visual acuity, Landolt C optotype and Snellen chart were employed. To participate, participants must have a best-corrected vision of at least 20/100, refraction errors were

measured using (Topcon automated keratorefractometer). Goldmann applanation tonometry was used to measure intraocular pressure, and examination of ocular motility in all directions of gaze has been done.

2.3. Laboratory investigations

They included the following

Diabetic profile, including glycated hemoglobin (HbA1c) and fasting blood sugar.

Kidney profile including blood urea and serum creatinine

Lipid profile including cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein.

2.4. Statistical analysis

Statistical analysis and data processing were done using a statistical package (IBM SPSS Statistics version 25.0; IBM Corporation, Armonk, New York, USA) for Windows. The histogram and the Shapiro–Wilk test were used to examine the degree of variation in normalcy. For categorical variables, we used numbers and percentages, whereas for continuous variables, we used means, ranges, and SD. For comparing the means of continuous data, we used the Student t test, and for categorical variables, we used the χ^2 test. The paired t test was used to make suitable comparisons between groups for variables that may be considered continuous. The diabetic and control groups were compared using the Mann–Whitney U test. The CC flow area and patient demographics were compared using Pearson's correlation coefficient test. The P value cutoff for all statistical tests was set at 0.05.

3. Results

The diabetic group's age varied from 30 to 60 years, with a mean ± SD age of 54.95 ± 7.87 years. Between groups A and B, there was no discernible difference in sex of the patients ($P > 0.05$). Patients had higher levels of fasting blood sugar and HbA1c than controls ($P = 0.05$) when it came to sugar profiles. The average number of years with DM was 12.32 ± 4.47, ranging from 8 to 25 years (Table 1).

There was no significant difference between case and control groups regarding ophthalmic data ($P > 0.05$), as shown in Table 2.

Regarding vessel density of choriocapillaris, there was a significant reduction in vessel density in the case group than in the control group ($P < 0.05$); however, there was no significant change in flow area between 3-mm-diameter and 6-mm-diameter in both groups ($P > 0.05$), as shown in Table 3.

Regarding flow area of choriocapillaris, there was a significant reduction in flow area in the case group than in the control groups ($P < 0.05$). Moreover, there was a significant difference in flow area between 3 and 6-mm-diameter in both groups ($P > 0.05$), as shown in Table 4.

There was a significant inverse correlation associating 3-mm-diameter flow area and vessel density of choriocapillaris with HbA1c ($P < 0.05$), whereas there was no significant correlation associating 3-mm-diameter flow area and vessel density of

Table 1. Comparison between case and control groups regarding demographic data and sugar profile.

	Group A	Group B	*P* value
Age (years)			
Mean ± SD (range)	54.95 ± 7.87 (30–60)	49.33 ± 7.17 (30–58)	0.231
Sex [*n* (%)]			
Male	8 (42.1)	5 (33.3)	0.435
Female	11 (57.9)	10 (66.7)	
Sugar profile [mean ± SD (range)]			
FBS (mg/dl)	133.74 ± 76.01 (85–345)	90.21 ± 9.15 (77–105)	0.018*
HbA1c (%)	8.15 ± 2.08 (5.70–12.57)	5.08 ± 0.56 (4.2–6)	0.001*
Duration of DM (years)	12.32 ± 4.47 (8–25)	NA	–

DM, diabetes mellitus; FBS, fasting blood sugar; HbA1c, glycated hemoglobin.
* = significant P value (P < 0.05).

Table 2. Comparison between case and control groups regarding ophthalmic data.

Ophthalmic data	Group A		*P* value
	Mean ± SD (range)	Group B [mean ± SD (range)]	
BCVA (log mar)	0.87 ± 0.12 (0.5–1)	0.93 ± 0.05 (0.8–1)	0.253
UCVA (log mar)	0.68 ± 0.11 (0.1–0.8)	0.73 ± 0.21 (0.3–1)	0.397
IOP (mmHg)	15.97 ± 2.92 (10–20)	16.53 ± 2.03 (12–20)	0.265

BCVA, best-corrected visual acuity; IOP, intraocular pressure; UCVA, uncorrected visual acuity.
* = significant P value (P < 0.05).

Table 3. Comparison between case and control groups regarding vessel density of choriocapillaris.

Vessel density (%)	Group A		P value[1]
	Mean ± SD (range)	Group B [mean ± SD (range)]	
3-mm-diameter	0.609 ± 0.49 (0.505–0.701)	0.663 ± 0.046 (0.576–0.754)	0.001*
6-mm-diameter	0.621 ± 0.051 (0.523–0.709)	0.666 ± 0.043 (0.584–0.756)	0.001*
P value[2]	0.332	0.816	

P^1 = change in vessel density between cases and controls.
P^2 = change in vessel density between 3 and 6-mm-diameter.
* = significant P value (P < 0.05).

Table 4. Comparison between case and control groups regarding flow area of choriocapillaris.

Flow area (mm^2)	Group A		P value[1]
	Mean ± SD (range)	Group B [mean ± SD (range)]	
3-mm-diameter	1.907 ± 0.157 (1.588–2.205)	2.086 ± 0.146 (1.812–2.373)	0.001*
6-mm-diameter	3.817 ± 0.309 (3.222–4.389)	4.047 ± 0.25 (3.547–4.550)	0.001*
P value[2]	0.001*	0.001*	

P^1 = change in flow area between cases and control.
P^2 = change in flow area between 3 and 6-mm-diameter.
* = significant P value (P < 0.05).

Table 5. Correlation between 3-mm-diameter flow area and vessel density of choriocapillaris with demographic data of studied patients.

3-mm-diameter	Vessel density (%)		Flow area (mm^2)	
	r	P value	r	P value
Age of patients	0.075	0.760	0.038	0.878
Duration of DM	−0.030	0.904	−0.054	0.827
FBS	−0.296	0.218	−0.274	0.265
HbA1c	−0.472	0.041*	−0.427	0.048*

DM, diabetes mellitus; FBS, fasting blood sugar; HbA1c, glycated hemoglobin.
* = significant P value (P < 0.05).

choriocapillaris with other demographic data of studied patients ($P > 0.05$), as shown in Table 5.

There was a significant inverse correlation associating 6-mm-diameter flow area and vessel density of choriocapillaris with HbA1c ($P < 0.05$), whereas there was no significant correlation associating 6-mm-diameter flow area and vessel density of choriocapillaris with other demographic data of studied patients ($P > 0.05$), as shown in Table 6.

There was no significant relation correlating flow area and vessel density of choriocapillaris with sex of studied patients ($P > 0.05$), as shown in Table 7.

Table 6. Correlation between 6-mm-diameter flow area and vessel density of choriocapillaris with demographic data of studied patients.

6-mm-diameter	Vessel density (%)		Flow area (mm^2)	
	r	P value	r	P value
Age of patients	0.020	0.935	0.064	0.794
Duration of DM	−0.087	0.723	−0.085	0.729
FBS	−0.317	0.187	−0.370	0.119
HbA1c	−0.458	0.049*	−0.471	0.042*

DM, diabetes mellitus; FBS, fasting blood sugar; HbA1c, glycated hemoglobin.
* = significant P value (P < 0.05).

4. Discussion

To assess the CC perfusion, 60 eyes from 34 participants were divided into two groups: group A included 30 eyes from 19 patients with NPDR, and group B included 30 eyes from 15 age-matched healthy participants who served as the control group. Finally, we discovered that both 3 and 6-mm-diameter scans of the cases group showed a substantial decrease in flow regions and vessel density compared with the control groups.

According to our findings, research examining perfusion density at the CC has shown variations between DM, DR, and non-DM individuals.[8]

In the observational cross-sectional research by Wang and Tao,[9] 104 eyes were divided into four groups. This study included healthy controls ($n = 38$ eyes), patients with DM ($n = 22$ eyes), patients with DR ($n = 24$ eyes), patients with nonproliferative disease ($n = 24$), and patients with proliferative disease ($n = 20$ eyes). Diabetic patients had their choroidal features and the presence of DR examined using OCT (DM). The following were their findings: patients with diabetes who had their eyes examined showed lower luminal to choroidal area (L/C ratio) than normal controls, as well as an increase in subfoveal choroidal thickness. The L/C ratio decreased significantly with the severity of DR eyes when compared with DM and normal eyes, suggesting that changes in the L/C ratio may help predict the development of DR.[9]

Using spectral-domain OCTA imaging, Conti et al.[10] performed a comprehensive chart review on 136 eyes. Nondiabetic controls ($n = 37$), patients with DM without DR (DM without DR, $n = 31$),

Table 7. Relation between flow area and vessel density of choriocapillaris with sex of studied patients.

	Male	Female	*P* value
	Mean ± SD (range)		
Vessel density (%)			
3-mm-diameter	1.917 ± 0.174 (1.588–2.205)	1.894 ± 0.137 (1.718–2.116)	0.701
6-mm-diameter	3.809 ± 0.269 (3.490–4.290)	3.823 ± 0.344 (3.220–4.390)	0.886
Flow area (mm^2)			
3-mm-diameter	0.612 ± 0.44 (0.546–0.673)	0.614 ± 0.049 (0.530–0.674)	0.782
6-mm-diameter	0.622 ± 0.045 (0.569–0.692)	0.626 ± 0.053 (0.543–0.691)	0.886

patients with NPDR ($n = 41$), and patients with PDR were the ocular groups studied (PDR, 27 eyes). For all patients and when comparing groups, quantitative analyses of OCTA pictures were done to determine the perfusion density of the CC and retinal plexus. In eyes with DR, they observed lower macular CC density and decreased flow regions at the conclusion of the research.

Using the SS-OCTA system, Choi and colleagues examined the perfusion of the macular CC in 63 eyes from 32 normal participants, nine eyes from seven patients with PDR, 29 eyeballs from 16 patients with NPDR, and 51 eyes from 28 diabetic patients without retinopathy in a prospective and cross-sectional research. Most eyes with NPDR and most eyes with PDR showed either localized or widespread CC flow impairment, which was seen in most eyes.

Moreover, Forte et al.[11] and Dodo et al.[12] found that visual acuity and DR are connected to CC nonperfusion. The team came to the conclusion that choroidal nonperfusion, which is linked to a disturbed photoreceptor layer, is probably a factor in the pathophysiology of reduced vision.

Visual acuity and DR are connected to CC nonperfusion. The team came to the conclusion that choroidal nonperfusion, which is linked to a disturbed photoreceptor layer, is probably a factor in the pathophysiology of reduced vision.

In a second OCTA investigation, flow deficits were used to assess CC flow and shown to be associated with decreased visual performance in DR eyes.[8,13,14]

Similar research was undertaken by Gendelman et al.[13] on 160 eyes from 90 diabetic individuals, all of whom underwent SS-OCTA imaging to look at the relationship between DR severity and macular CC FD percent. They discovered a strong positive correlation between FD percent and DR severity. That is, there was a comparable rising deficiency in the CC as DR developed.

The preceding results could be accounted for by the fact that the initial NPDR-related changes are not microaneurysm development but rather changes to the retinal vasculature. Reduced capillary density in the perifoveal region, together with the noticed CC abnormalities, signal the onset of vascular changes in diabetes early on. These findings show that choroidal vascular abnormalities are present in patients with DM and worsen as DR advances, indicating that choroidal vascular abnormalities may represent an early-stage pathogenic event in the disease process itself.[15]

In our study, we used the Pearson's correlation coefficient test to compare the flow area and vessel density of choriocapillaris (3 and 6 mm in diameter) with the demographic information of the patients. We discovered a significant inverse correlation between the HbA1c and the flow area and vessel density of choriocapillaris (3 and 6 mm in diameter), which suggests that CC perfusion may be affected by the severity of the DM.

To the best of our knowledge, there has not been any research on the link between CC flow area and HbA1c; however, Shiba et al.[14] did an institutional evaluation on 196 patients to assess the changes in ocular blood flow of the retina and choroid in patients with DM (151 men, 45 women). Choroid and HbA1c levels in people with and without diabetes were measured to see whether there were any correlations. Choroid blood flow was shown to be substantially linked with HbA1c levels in diabetics, according to the findings. An association between elevated HbA1c levels and decreased choroid and eye blood flow has been discovered, which may shed light on the etiology of DR and its progression.[14]

In addition, a cross-sectional investigation was carried out by Nagaoka et al.[16] on 194 eyes with type 2 DM and 75 eyes that were not diabetic. Two groups of type 2 diabetic eyes were identified: 55 eyes (55 patients) with NPDR and 139 eyes (139 patients) without DR. Laser Doppler velocimetry was used to evaluate the retinal circulatory parameters, and patients with type 2 diabetes were studied to identify the variables that influence the retinal hemodynamics. They came to the conclusion that HbA1c was considerably greater among diabetic individuals with the lowest RBF, indicating that the decline in RBF is linked to inadequate glycemic management.[16]

Poorly regulated HbA1c may be linked to more advanced stages of DR as a result of decreased choroidal blood flow and choroidal hypoxia, which may contribute to choroidal thinning. The research was carried out with an eye on the future.

Using HbA1c levels as a guide, Torabi et al.[17] examined the eyes of 180 persons with type 2 diabetes and divided them into three categories: those with good glucose control (HbA1c 7%), those with intermediate glycemic control (HbA1c 7–8%), and those with poor glucose control (HbA1c >8%). Using spectral-domain OCT, choroidal thickness was measured and compared in individuals with type 2 DM to determine the relationship between HbA1c levels and choroidal thickness. Patients with poor glycemic control (HbA1c >7%) had choroidal thicknesses that were considerably lower than those in the healthy control group, but the thicknesses in the better-controlled diabetics were practically identical. (HbA1c 7%). When blood sugar levels are below 7%, it may be possible to reduce the risk of developing DR.

4.1. Conclusion

Patients with NPDR experienced a significant reduction in CC blood flow in the macular region, and HbA1c also had an effect on CC blood flow, indicating that patients with NPDR and poor glycemic control may also experience significant CC blood flow impairment. Patients with DR may benefit from OCTA because of its capacity to identify retinal and CC microvascular abnormalities, as well as new insights into pathophysiology, treatment response, and an earlier diagnosis of vascular abnormalities.

Consent statement

Patient's consent was obtained before being included in the study.

Conflict of interest

The authors report no conflicts of interest in this work.

References

1. Eisma JH, Dulle JE, Fort PE. Current knowledge on diabetic retinopathy from human donor tissues. *World J Diabetes*. 2015; 6:312–320.
2. Wang W, Lo A. Diabetic retinopathy: pathophysiology and treatments. *Int J Mol Sci*. 2018;19:1816.
3. Romero-Aroca P, Baget-Bernaldiz M, Pareja-Rios A. Diabetic macular edema pathophysiology: vasogenic versus inflammatory. *J Diabetes Res*. 2016;16, 2156273.
4. Nittala MG, Keane PA, Zhang K. Risk factors for proliferative diabetic retinopathy in a Latino American population. *Retina*. 2014;34:1594–1599.
5. Spaide RF, Fujimoto JG, Waheed NK. Optical coherence tomography angiography. *Prog Retin Eye Res*. 2018;64:1–55.
6. Duh EJ, Sun JK, Stitt AW. Diabetic retinopathy: current understanding, mechanisms, and treatment strategies. *JCI Insight*. 2017;2, e93751.
7. Agemy SA, Scripsema NK, Shah CM. Retinal vascular perfusion density mapping using optical coherence tomography angiography in normal and in diabetic retinopathy patients. *Retina*. 2015;35:2353–2363.
8. Moir J, Khanna S, Skondra D. Review of OCT angiography findings in diabetic retinopathy: insights and perspectives. *Int J Transl Med*. 2021;1:286–305.
9. Wang H, Tao Y. Choroidal structural changes correlate with severity of diabetic retinopathy in diabetes mellitus. *BMC Ophthalmol*. 2019;19:186.
10. Conti FF, Qin VL, Rodrigues EB. Choriocapillaris and retinal vascular plexus density of diabetic eyes using split-spectrum amplitude decorrelation spectraldomain optical coherence tomography angiography. *Br J Ophthalmol*. 2018; 103:452–456.
11. Forte R, Haulani H, Jürgens I. Quantitative and qualitative analysis of the three capillary plexuses and choriocapillaris in patients with type 1 and type 2 diabetes mellitus without clinical signs of diabetic retinopathy: a prospective pilot study. *Retina*. 2018;40:333–344.
12. Dodo Y, Suzuma K, Ishihara K. Clinical relevance of reduced decorrelation signals in the diabetic inner choroid on optical coherence tomography angiography. *Sci Rep*. 2017;7:5227.
13. Gendelman I, Alibhai AY, Eric M, Moult EM. Topographic analysis of macular choriocapillaris flow deficits in diabetic retinopathy using swept–source optical coherence tomography angiography. *Int J Retina Vitreous*. 2020;6:6.
14. Shiba C, Shiba T, Takahashi M. Relationship between glycosylated hemoglobin A1c and ocular circulation by laser speckle flowgraphy in patients with/without diabetes mellitus. *Graefes Arch Clin Exp Ophthalmol*. 2016;254:1801–1809.
15. Choi W, Waheed NK, Moult EM. Ultrahigh speed swept source optical coherence tomography angiography of retinal and choriocapillaris alterations in diabetic patients with and without retinopathy. *Retina*. 2017;37:11–21.
16. Nagaoka T, Sato E, Takahashi A. Impaired retinal circulation in patients with type 2 diabetes mellitus: retinal laser Doppler velocimetry study. *Invest Ophthalmol Vis Sci*. 2010;51: 6729–6734.
17. Torabi H, Saberi Isfeedvajani M, Ramezani M. Choroidal thickness and hemoglobin A1c levels in patients with type 2 diabetes mellitus. *J Ophthalmic Vis Res*. 2019;14:285–290.