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Choroidal Changes in Diabetic Patients with Different Stages of Diabetic Retinopathy

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ABSTRACT

Background: Choroidal and retinal vascular density (VD) can be evaluated without using any dye with optical coherence tomography angiography (OCT**A**) through motion contrasting.

Objective: This study aimed to assess choroidal changes in solid versus diabetic-retinopathy (DR) patients with/without differed seriousness of DR.

Methods: This controlled prospective non-randomized study was carried through the period from April 2021 to April 2022 in Al-Azhar University Hospital, Assiut branch.

Results: Raise in Foveal Avascular Zone (FAZ) area in diabetic-retinopathy patients directly proportional to the retinopathy severity and decrease after pan-retinal-photo coagulation. While there is decrease in retinal, choroidal thickness and vessel density in diabetic-retinopathy patients directly proportional to the retinopathy severity and increase after pan retinal photo coagulation.

Conclusion: OCTA identified as pre-clinical DR before the aspect of clinical retinopathy due to the prospect role in monitoring and quantifying retinal and choroidal vascular alterations of diabetes.

Keywords: OCT, Angiography, Choroidal, Retina, Diabetic, Retinopathy.

INTRODUCTION

Diabetic retinopathy (DR) is considered a significant vision undermining issue and which causes vision misfortune among the working-age populace overall and to that end it is an overall medical condition with monetary contemplations in addition to its exorbitant administration. By 2040, approximately 145 million patients will have varying degrees of DR, and this number will nearly double [(1)].

Clinical and experimental research has shown that choroidal changes are obtained in different of retinal pathologies, have a vital function in the progression of diabetic retinopathy [(2)]. Diabetic retinopathy has been accounted for that diabetic patients have modified choroidal dissemination with expanded pulsatile visual blood stream [(3)]. A few neurotic changes in the choroidal vasculature were viewed as indistinguishable from those in DR patients' retinal blood vessels [(4)].

Depth imaging mode and spectral domain optical coherence tomography (EDI SD-OCT) were used to identify the choroidal thickness (CT) of diabetic patients with DR. In some studies, CT was found to be higher in DR patients than in controls, while in others, CT was found to be lower as DR severity increased and there was no linkage between choroidal thickness and diabetic retinopathy [(5-9)].

Swept source optical coherence tomography (SS-OCT) is a novel method that provides CT measurements that are more consistent and reliable than those made using EDI SD-OCT [(10)]. This is because of the more obvious choroid-scleral interface.

By detecting the motion of blood cells within the blood vessels, high-speed optical coherence tomography and a splits spectrum amplitude-decorrelation angiography algorithm (SSADA) were used to non-invasively capture images of the retinal and choroidal blood vessels. From high-goal volumetric blood stream information, this state-of-the-art imaging procedure rapidly creates angiograms. In vivo studies of human ocular microcirculation using SSADA have been successful [(11)].

Thus, this study purposed to determine choroidal changes in solid versus diabetic-retinopathy patients with/without differed seriousness of diabetic retinopathy.

PATIENTS AND METHODS

This prospective, non-randomized study included 120 eyes of solid and diabetic people with various phases of diabetic retinopathy from the short-term eye facilities of Al-Azhar College Emergency Clinic, Assiut branch.

Inclusion criteria: Type 2 diabetes mellitus in both sexes, 30-70 years old, with normal IOP and visual acuity of 0.1 decimal or better and no other intraocular disease.

Exclusion Criteria:

Patients who have a history of glaucoma or cataracts, vitreous hemorrhage, retinal detachment, a refractive error of more than +6D or -6D, previous retinal laser therapy (with the exception of the last group), intravitreal injections or intraocular surgery that was performed within six months of the OCT assessment, and a history of severe systemic illness that is complicated by significant fluid retention such as hypertension, cardiovascular disease, inadequate OCT images as a result of severe pathology or unstable fixation.

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Before any procedures were performed, each patient underwent a thorough examination to identify eye disorders and medical history. Each set of eyes' uncorrected and best revised visual sharpness (BCVA) were assessed utilizing a decimal outline and Log Blemish units. All patients were exposed to the resulting steps:

1. History: **Systemic:** The medical histories and illnesses of all participants were looked at. We inquired about their HbA1c levels, commitment to diabetes management, and duration of diabetes. **Ocular:** information about visual history, which included things like past eye wounds, medical procedures, remedy glasses, and eye drops, particularly those for glaucoma. Vitreous hemorrhage, retinal detachment, intraocular anti-VEGF injections, pan retinal photocoagulation, and any kind of retinal laser were heavily emphasized during the ocular history.

2. **Evaluation:** used to examine the anterior and posterior segments for the dilated fundus examination, and an applanation tonometer was used to measure intraocular pressure for all participants. Fluorescein angiography and OCT were finished for all diabetic members to decide the phase of DR and the focal macular thickness (macular edema or not).

3-Imaging:

Figure (1): The Topcon DRI OCT Triton [(11)]

DRI Triton (Topcon, Tokyo, Japan) Figure (1), which features a 1,050-nm-wavelength swept light source and a scanning speed of 100,000 A-scans/second, was used for all study participants' simultaneous (SS)-OCT and OCTA examinations, included:

a) Retinal thickness utilizing a six-line spiral example filter (1,024 A-examines focused on the fovea)

b) Choroidal thickness estimated at 2 millimeters from the fovea (nasal, worldly, unrivaled, and mediocre).

c) Quantitative measurement of the Foveal Avascular Zone (FAZ) at the SCP using a 3 x 3 mm scan.

d) Qualitative analysis of the parafoveal area at the SCP and DCP using a 4.5 x 4.5 mm scan.

e) Quantitative measurement of the density map of retinal vessels at the SCP using a 4.5 x 4.5 mm scan.

f) Measuring the density map of choroidal vessels.

Ethical Consideration: The review endorsed by Al-Azhar Morals Board of trustees and was finished in accordance with Helsinki Announcement. Before entering the study, each participant provided an informed consent.

Statistical Analysis

Collected data were revised, coded, and tabulated using IBM SPSS 20.0. The data were presented and the appropriate analysis was performed based on the type of data obtained for each parameter. ANOVA was used to determine the statistical significance of a parametric variable's mean difference between more than two study groups. A pairwise test was used to see if a group was statistically significant.

RESULTS

Table (1) Regarding gender, there was no statistically significant difference between the five groups.

Table (1): Comparison between the studied groups regarding demographic characteristics.

	Group 1 Control group		Group 2 DM without DR	Group 3 NPDR	Group 4 PDR	Group 5 Post PRP	Test value	P-value
Age (years)	**Mean ± SD**		**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	KW= 14.22	**0.007**
	49.60 ± 10.65		50.68 ± 10.78	53.0 ± 10.0	55.64 ± 9.47	59.32 ± 6.77		
Gender	**Male**	8 (40.0%)	10 (40.0%)	13 (52.0%)	11 (44.0%)	11 (44.0%)	X^2= 0.939	0.919
	Female	12 (60.0%)	15 (60.0%)	12 (48.0%)	14 (56.0%)	14 (56.0%)		

Table (2) shows: The mean duration of DM was 6.20± 2.77 years in DM without DR group, 12.32± 2.17 years in NPDR group, 14.36± 3.51 years in PDR group and 18.28± 4.29 years in Post PRP group. Pan-retinal photocoagulation (PRP) was significantly done only in patients of post PRP group.

Table (2): Comparison between the studied groups regarding clinical characteristics

	Group 1 Control group		Group 2 DM without DR		Group 3 NPDR		Group 4 PDR		Group 5 Post PRP		Test value	P-value
Duration of DM (years)	**Mean ± SD**		**Mean ± SD**		**Mean ± SD**		**Mean ± SD**		**Mean ± SD**		KW= 64.78	**<0.001**
	0		6.20 ± 2.77		12.32 ± 2.17		14.36 ± 3.51		18.28 ± 4.29			
PRP NO	20 (100.0%)		25 (100.0%)		25 (100.0%)		25 (100.0%)		0 (0.0%)		X^2= 120.0	**<0.001**
PRP Yes	0 (0.0%)		0 (0.0%)		0 (0.0%)		0 (0.0%)		25 100.0%)			
NO of IVI	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	**Mean**	**± SD**	KW= 5.80	0.055
	0	0	0	0	1.60	1.44	2.32	2.08	3.0	2.04		

Table (3) showed that a significant difference was found between the five groups regarding Visual Acuity LOG MAR (p-value < 0.001).

Table (3): Comparison between the studied groups regarding visual acuity

	Group 1 Control	Group 2 DM without DR	Group 3 NPDR	Group 4 PDR	Group 5 Post PRP	Test value	P-value
Visual Acuity LOG MAR	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	KW= 55.14	**<0.001**
	0.17 ± 0.19	0.17 ± 0.12	0.30 ± 0.30	0.66 ± 0.28	0.66 ± 0.30		

Table (4) showed that foveal thickness values were significantly different among the five groups and all pairwise comparisons were statistically significant except between control group and DM without DR group.

Table (4): Comparison between the studied groups regarding retinal thickness

Group / Thickness in (µm)	Group 1 Control	Group 2 DM without DR	Group 3 NPDR	Group 4 PDR	Group 5 Post PRP	Test value	P-value
	Mean ± SD	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**	**Mean ± SD**		
Foveal Thickness	239.7 ± 10.87	238.4 ± **0**.85	233.9 ± **0**.47	203.85 ± 23.0	223.72 ± 11.4	KW= 87.44	**<0.001**
Superior para foveal	312.2 ± 6.22	309.4 ± 8.89	307.68 ± 8.16	295.0 ± 14.56	298.08 ± 8.10	KW= 32.81	**<0.001**
Inferior para foveal	293.68 ± 16.4	293.5 ± 11.85	291.88 ± 15.02	289.5 ± 19.34	290.5 ± 8.13	F= 0.279	0.891
Nasal para foveal	302.5 ± 5.36	299.4 ± 17.06	293.3 ± 9.72	288.96 ± 7.23	291.96 ± 6.85	KW= 15.36	**0.007**
Temporal para foveal	297.4 ± 19.37	296.1 ± 9.50	293.4 ± 19.37	284.48 ± 18.56	291.47 ± 19.1	KW= 23.64	**<0.001**

Table (5) showed that sub-foveal choroidal thickness values were significantly different among the five groups. Superior and temporal choroidal thickness values were significantly different among the five groups. Inferior choroidal thickness values were significantly different among the five groups. Significant difference among the five groups. PDR group had significant thinner nasal choroidal thickness compared to control group, non-diabetic retinopathy and NPDR group (p value< 0.001, <0.001& 0.013 respectively). DM post PRP had significant thinner nasal choroidal thickness compared to control group and non-diabetic retinopathy, NPDR groups (p value=0.004, < 0.001&0.033 respectively).

Table (5): Comparison between the studied groups regarding choroidal thickness

Choroidal thickness in(µm)	Group 1 Control group	Group 2 DM without DR	Group 3 NPDR	Group 4 PDR	Group 5 Post PRP	Test value	P-value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
Sub foveal choroidal thickness	312.75 ± 20.97	299.21 ± 20.87	296.98 ± 53.94	232.31 ± 9.72	253.86 ± 9.18	F= 34.39	**<0.001**
Superior choroidal thickness	265.80 ± 7.15	229.08 ± 1.12	224.16 ± 2.06	195.88 ± 14.58	213.42 ± 3.49	KW= 111.07	**<0.001**
Inferior choroidal thickness	260.15 ± 11.76	235.58 ± 1.30	225.39 ± 42.11	174.84 ± 7.41	198.66 ± 9.84	KW= 105.45	**<0.001**
Nasal choroidal thickness	258.55 ± 26.63	233.96 ± 1.89	218.51 ± 2.10	187.00 ± 20.36	191.35 ± 8.42	KW=4 4.62	**<0.001**
Temporal choroidal thickness	269.50 ± 25.57	222.22 ± 40.78	231.40 ± 1.87	187.28 ± 41.95	212.55 ± 29.51	KW= 99.89	**<0.001**

Table (6) showed FAZ area were significantly different among the five groups except between " control vs non-diabetic retinopathy " as well as " NPDR group Vs Post PRP group " that showed no significant difference. In addition, superior and nasal retinal density values were significantly different among the five groups. Inferior and temporal retinal density values were significantly different among the five groups except between control vs nondiabetic retinopathy & NPDR vs post PRP groups in inferior retinal density and between control vs non-diabetic retinopathy in temporal retinal density.

Table (6): Comparison between the studied groups regarding retinal density map

	Group 1 Control	Group 2 DM without DR	Group 3 NPDR	Group 4 PDR	Group 5 Post PRP	Test value	P-value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
FAZ area	0.29 ± 0.01	0.29 ± 0.03	0.41 ± 0.03	0.48 ± 0.03	0.36 ± 0.08	KW= 83.38	**<0.001**
Superior retinal density	55.69 ± 0.34	53.18 ± 1.11	52.16 ± 0.88	42.54 ± 2.72	45.75 ± 2.34	KW= 105.37	**<0.001**
Inferior retinal density	56.55 ± 1.02	54.32 ± 1.57	51.61 ± 0.86	41.39 ± **0**.74	44.87 ± 1.26	KW= 93.81	**<0.001**
Nasal retinal density	48.12 ± 0.76	46.05 ± 0.68	45.6 ± 0.75	42.35 ± 2.02	45.79 ± 1.45	KW= 108.77	**<0.001**
Temporal retinal density	53.41 ± 1.04	52.73 ± 0.83	50.47 ± 0.70	42.39 ± 2.10	44.72 ± 0.94	KW= 109.17	**<0.001**

As regard nasal and temporal choroidal density values, they were significantly different among the five groups except between non-diabetic retinopathy vs NPDR vs post PRP groups that showed no significant difference (Table 7).

Table (7): Comparison between the studied groups regarding choroidal density map

	Group 1 Control group	Group 2 DM without DR	Group 3 NPDR	Group 4 PDR	Group 5 Post PRP	Test value	P-value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD		
Superior choroidal density	50.70 ± **0**.42	48.53 ± 1.37	44.31 ± 1.47	40.22 ± 3.58	45.80 ± 2.38	KW= 92.89	<**0.001**
Nasal choroidal density	48.84 ± 2.57	45.99 ± 1.13	44.78 ± 1.92	37.99 ± 2.61	43.83 ± 1.34	KW= 90.23	<**0.001**
Inferior choroidal density	54.31 ± 2.31	49.12 ± **0**.67	45.30 ± 1.15	42.21 ± 0.74	44.57 ± 1.37	KW= 105.5	<**0.001**
Temporal choroidal density	57.92 ± 3.33	47.55 ± 1.36	46.98 ± 0.84	40.37 ± 2.06	45.42 ± 1.62	KW= 93.84	<**0.001**

DISCUSSION

Diabetes is an endocranial condition that affects the blood vessels throughout the body. Although the retinal vasculature undergoes the majority of changes in diabetic eyes [12]. High-resolution imaging of improve and identify blood flow and structure of choroidal and retinal, OCTA have the ability to identify the microvasculature of diabetic retinopathy [13]. Increased tortuosity, focal vascular dilation or narrowing, the formation of sinus-like structures between the choroidal lobules, luminal tightening of the capillaries, capillary wipeout, and minute scarring are all observed in histologic studies of diabetic eyes [14]. In addition to choroidal neo-vascular, saccular-dilatation, micro-aneurysms in the choroidal capillaries, filling delay or defects [15]. In agreement with our results **Sudhalkar *et al.*** [16] a direct correlation between the severity of diabetic retinopathy and choroidal thickness in diabetic patients with diabetic-retinopathy were increasing, although reported by **Esmaeelpour *et al.*** [17]. On the other hand, a Korean hospital-based study by **Kim *et al.*** [18] reported that the exact mechanism for the observed increase in choroidal thickness in diabetic-retinopathy patients is unknown.

Nagaoka *et al.* [19] found a decrease in choroidal thickness before diabetic-retinopathy was present. Additionally, color doppler imaging of posterior ciliary arteries significantly reduces choroidal circulation in diabetic-retinopathy patients as mentioned by **Dimitrova *et al.*** [20]

As previously mentioned in two studies by **Schocket and coworkers** [21], as well as **Di *et al.*** [22] retinal tissue hypoxia and VEGF overexpression may cause choroidal hypoperfusion to initiate DR. In patients with PDR, both choroidal blood flow and volume are significantly reduced.

Furthermore, **Takahashi *et al.*** [23] noted that the mean choroidal blood volume and choroidal blood flow values significantly increased after PRP, in addition our study observed an increase in choroidal and retinal thickness, vessel density, and blood flow in sever diabetic retinopathy. **Cho *et al.*** [24] choroidal-thickness PRP treatment resulted in significant increases in SFCT. They demonstrated that in eyes without macular edema and severe diabetic retinopathy, argon laser PRP results in a significant SFCT. According to **Abdelhalim *et al.*** [25] PRP significantly improved OCTA parameters in PDR patients. In patients with PDR, it is known that PRP reduces cytokines, which increase vascular permeability and dropout, decrease posterior pole, and cause macular ischemia and an increase in the FAZ area [26].

Lorusso and colleagues [27] reported that OCTA boundaries not impacted by laser treatment at 1-month and a half year follow-up. This is in opposition to both our study and a study by **Faghihi *et al.*** [28] that reported an increase of vascular density in the foveal region, the vascular density in the parafoveal and foveal regions with non-statistically significant changes.

CONCLUSION

OCTA identified as pre-clinical DR before the aspect of clinical retinopathy due to the prospect role in monitoring and quantifying retinal and choroidal vascular alterations of diabetes.

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