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Indian Journal of Clinical and Experimental Ophthalmology

Journal homepage: www.ijceo.org

Original Research Article

Choroidal thickness in type 2 diabetes mellitus patients using spectral domain optical coherence tomography

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ARTICLE INFO

Article history:
Received 02-07-2023
Accepted 21-07-2023
Available online 30-09-2024

Keywords:
Diabetes mellitus
Choroidal thickness
Coherence tomography

ABSTRACT

Aim: To measure the choroidal thickness in patients with type 2 diabetes mellitus and its comparison to healthy age-matched individuals.

Materials and Methods: This prospective comparative study conducted at departments of Ophthalmology, Shri B.M. Patil Medical College, Hospital and Research Centre, Vijayapura. Study included 192 patients, 96 with diabetes and 96 age-matched controls. Data acquired comprised demographics, a thorough eye examination, fundus photography and spectral domain optical coherence tomography measurements of choroidal thickness using enhanced depth imaging.

Results: Mean age was 60.17±7.727 years with male predominance in both cases and controls. The mean duration of diabetes was 5.67±3.39 years. Positive correlation was noted between duration of diabetes and severity of retinopathy (p = 0.001). 21 patients did not have any evidence of diabetic retinopathy, while 75 patents had features of non-proliferative diabetic retinopathy, of which (31) had mild, (21) moderate, (12) severe and (11) with proliferative diabetic retinopathy. Mean choroidal thickness of controls was 327.308±18.945 microns, as compared to thinner choroids 295±15.082 microns in cases without retinopathy and 271 ± 36.122, 242 ±30.048, 193±15.748 microns in mild, moderate, severe non-proliferative diabetic retinopathy respectively and 191.492± 23.834 microns in proliferative diabetic retinopathy. Statistically significant differences were noted on comparing choroidal thickness between controls and cases (p = 0.001).

Conclusion: Choroidal thickness was maximum in control group with a p value of <0.001, while cases showed overall thinner choroids with increasing severity of retinopathy. Thinnest choroids were observed in patient with proliferative diabetic retinopathy. Choroidal thickness can be used as a non-invasive prognostic bio marker for diabetic retinopathy.

1. Introduction

Diabetes mellitus (DM) is a significant public health problem where more than 300 million people are affected, with severe morbidity and mortality. Its long-term complications can decrease patients' quality of life.[1] DM is among the top 10 leading causes of death, and a significant global health emergency. By 2035, it is projected that diabetes will take the lives of about 592 million people.[2,3] One of the main reasons for preventable blindness in working-age adults is diabetic retinopathy, affecting more than 35% of diabetic patients, as the choroid being a vascular structure, is exceptionally vulnerable to both microvascular and macro-vascular abnormalities caused by type 2 DM. Rajiv Raman et al. estimated that 12.4% of Indians had diabetic retinopathy in 2022, of which 4% had vision-threatening diabetic retinopathy (VTDR). They also estimated that in 2022, three million Indians over 40 had

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https://doi.org/10.18231/j.ijceo.2024.082

VTDR.

Many recent studies have focused on choroidal thickness (CT) as an indicator of choroidal blood flow. The vascular layer of the eye is the choroid, often referred to as the choroid coat, which is positioned between the retina and sclera and receives a substantial amount of ocular blood flow. The choroid plays a significant role in providing nutrients to the outer retinal layers; any changes in choroidal structure and vasculature in the form of microvascular or macro-vascular abnormalities may vastly affect the retinal function.[4] It also provides nourishment to retinal pigment epithelium (RPE) and photoreceptors, whose maintenance is necessary for the exceptionally metabolically active photoreceptor cells, the lack of retinal blood vessels within foveal regions being the most notable example.[5] The fovea is the most sensitive area of the retina, responsible for sharp central vision and supplied by the choroidal vasculature, and thus also affected in choroidopathy. Damage of choriocapillaris may cause severe functional impairment to tissues in the foveal region.[6]

The choroid is responsible for providing sustenance to the outer layers of the retina, and any changes to the choroidal anatomy or vasculature may impact retinal function.

The scientific and experimental data suggest that choroidal vascular abnormalities may contribute to the pathophysiology of diabetic retinopathy (DR) and retinal alteration. Previous research on diabetic eyes has noted a variety of choroidal anomalies, such as blockage of the choriocapillaris, vascular degeneration, choroidal aneurysms, and choroidal neovascularization.[6–8] Thus, such choroidal vascular irregularities can lead to severe complications and dysfunction of the outer retina. However, in recent times, very few studies have been carried out on choroidal vasculature assessment and associating features. Thus, this study aims to assess the choroid thickness variations secondary to diabetic-induced vasculature abnormalities in patients with diabetes mellitus.

Choroidal imaging has seen a lot of development in recent years. Previously invasive procedures such as indocyanine green angiography were used for the imaging and assessment of the choroid, which made it difficult to carry out studies of choroidal pathology at a large scale. However, a more non-invasive and convenient method for choroidal imaging has emerged in recent years. Since the invention of spectral domain optical coherence tomography (SD-OCT), the imaging of the choroid has been gradually improving. SD-OCT enhanced depth imaging (EDI) has also made it possible to visualize and image the choroid more clearly.[9] The ability to track one's fovea makes optical coherence tomography with enhanced depth imaging (EDI OCT) unique in that it can quantify the thickness of the choroid in both healthy and diseased conditions.[9–11]

2. Materials and Methods

This prospective comparative and time-limited study was conducted at the Department of Ophthalmology, BLDE (DU) Shri B.M. Patil Medical College, Hospital and Research Centre Vijayapura, Karnataka. After appropriate intuitional ethical clearance (IEC/NO-09/2021) from the institutional ethical committee and patient consent, the study was conducted from November 2020 to May 2022. It included 192 patients, 96 patients with Type 2 Diabetes Mellitus and 96 age-matched controls. Patients having a history of type 2 diabetes mellitus met the inclusion criteria for the study group. Individuals having type 1 diabetes mellitus, a history of treatment for diabetic retinopathy, high myopes and developmental anomalies increasing axial length, conditions causing hazy media and other retinal pathologies were exclusion criteria.

A detailed history was obtained that included demographic details, duration of diabetes, diabetic control and treatment history. A comprehensive ophthalmological examination was also carried out, including best-corrected visual acuity (BCVA), intraocular pressure, slit lamp examination, fundus examination and fundus photography. Biochemical investigations included glycosylated haemoglobin (HbA1c) levels, random blood sugar (RBS), fasting blood sugar (FBS) and post-prandial blood sugar (PPBS) leaves. Using a commercial kit modified for an auto analyser, biochemical parameters were examined at a clinical biochemistry laboratory. Centrifugation was used to separate the serum for 10 minutes at 4,000 rpm. The plasma glucose level was calculated using the glucose oxidase and peroxidase (GOD-POD) endpoint assay technique.

After evaluation, patients in the study group were classified according to the early treatment diabetic retinopathy study (ETDRS) criterion into mild, moderate, severe non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) as shown in (fundus photograph of patient in the study group with proliferative diabetic retinopathy).(Figure 1)

2.1. Choroidal thickness measurements

To obtain retinal scans, SD-OCT was utilized; (ZEISS CIRRUS 500 HD-OCT). Scans were carried out without pupillary dilation using EDI mode. The thickness of the central sub-foveal choroid of each eye was evaluated with the available calliper (CIRRUS software version 8.0; ZEISS CIRRUS 500). Measurements were made between the choroid and the scleral interface and the highly reflective zone underneath the retinal pigment epithelium (RPE), corresponding to Bruch's membrane. Up to 3000 microns of temporal and nasal intervals at 500 microns each were captured. The middle horizontal B-scan cross-sectioned the foveal centre in a direct line. The central sub fovea was 500 m in the nasal and temporal directions based on choroidal

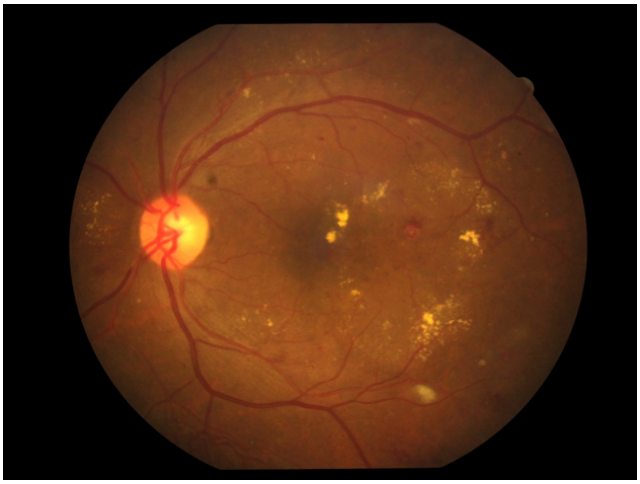

Figure 1: Fundus photograph of patient in the study group with proliferative diabetic retinopathy

thickness measures. Only scans with a signal strength greater than or equal to 6 were employed for analysis. Linear measurements were made using the inbuilt measurement tool on the cirrus OCT.

2.2. *Statistical analysis*

Specific statistical software for the social sciences was used for statistical analysis (Version 20). Graphs, counts, and percentages were also used to illustrate the results and the Mean and SD. To compare regularly distributed and continuous variables between two groups, independent t-tests were used, alongside the Mann-Whitney U test, when dealing with continuously skewed data was applied. Mean values of different variables of subgroups were compared using ANOVA/Kruskal Walli's test. Categorical variables between the two groups were compared using the Chi-square test. Statistical significance was determined by a P value < 0.05. All necessary statistical analyses were carried out.

3. Results

The study group consisted of 96 diabetic patients that fulfilled the criteria for analysis. The mean age of diabetic patients was 58.86 ±8.034, with a male predominance. On evaluation of the diabetic status of the study group, the mean duration of diabetes was 5.67± 3.39 years, with a majority of the patients 37(35.52%) having a history of diabetes of 5-10 years duration. In correlation with the severity of retinopathy, patients with mild NPDR had an average duration of less than five years, moderate NPDR of five to ten years, and severe NPDR of ten to fifteen years. The mean HbA1c levels were 7.86% ±2.786, with the highest above 8% in 22 patients with PDR and 21 with severe NPDR. The mild NPDR and moderate NPDR groups had the majority of patients with HbA1c between 6.5 to 7.9%. A comparison of biochemical and demographic characteristics between the study and control groups is given in Table 1.

Out of the 96 patients in the study group, 21 patients did not have any evidence of diabetic retinopathy, while 75 patients had features of diabetic retinopathy, of which (31) had mild NPDR, (21) had moderate NPDR, (12) had severe NPDR and (11) had PDR (Figure 2).

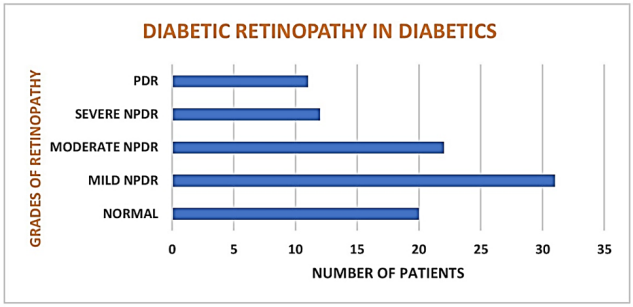

Figure 2: Distribution of grades of diabetic retinopathy in diabetic patients

The control group also comprised 96 healthy age-matched patients with an average age of 61.48 ±7.421 years with male predominance. Compared to the study group, mean HbA1c levels were markedly lower, with a mean of 4.7% ± 0.593 and P value of <0.001.

CT measurements of control group patients showed an overall mean choroidal thickness of 327.308± 18.945 microns compared to study group patients with thinner choroids and an overall mean thickness of 238.48 ± 24.127. Additionally, a general decline in CT was observed, with increasing severity or higher grades of diabetic retinopathy. In the study group, mean CT of 295 ±15.082 microns were observed in diabetic patients without retinopathy and 271 ± 36.122, 242 ± 30.048, 193 ±15.748 and 191.492 ± 23.834 microns were observed in mild NPDR, moderate NPDR, severe NPDR and PDR respectively (Table 2).

Subfoveal choroidal thinning was statistically significant (P < 0.001) in the study group of patients with retinopathy compared to patients without retinopathy. Study group patients had significantly thinner subfoveal CT in comparison to age-matched healthy patients in the control group (P < 0.001) (Kruskal-Wallis Test).

4. Discussion

The choroidal vasculature must be physically and functionally intact for the retina to operate correctly. Any abnormalities in the choroidal circulation and blood volume leading to a compromised choroidal blood flow can eventually cause the dysfunction of the photoreceptor leading to its death. DM, mainly targeting the microvasculature, can affect multiple systems. The retina, choroid and kidneys are majorly affected and can influence

Table 1: Table comparing various parameters between cases and controls

	Cases		Controls			
	Mean	**Standard devation**	**Mean**	**Standard devation**	**Mann-whitney u**	**P value**
Age	58.86	8.03	61.48	7.42	1241.000	<0.001
HbA1C	7.86	2.78	4.70	0.59	1067.000	< 0.001
PPBS	229.07	78.41	164.22	14.7	1524.000	<0.001
FBS	172.76	68.68	94.47	9.07	653.500	<0.001
Subfoval Thickness	253.63	36.35	328.30	18.11	350.500	<0.001

Table 2: Table showing comparisons of choroidal thickness between diabetic patients and controls

Choroidal thickness	**Groups**	**Mean choroidal thickness (μm)**	**Sd**	**Kruskal-wallis test**	**P value**
Subfoval	No Retinopathy	302.70	10.063	145.674	<0.001
	Mild NPDR	276.03	30.522		
	Moderate NPDR	239.68	31.242		
	Severe NPDR	195.08	12.972		
	PDR	193.00	15.245		
	Controls	328.30	17.382		
Nasal	No retinopathy	291.80	13.477	147.556	<0.001
	Mild NPDR	268.55	31.891		
	Moderate NPDR	231.73	30.376		
	Severe NPDR	188.83	13.630		
	PDR	186.09	15.527		
	Controls	324.88	18.117		
Temporal	No Retinopathy	297.70	11.150	148.509	<0.001
	Mild NPDR	272.13	30.407		
	Moderate NPDR	236.50	31.567		
	Severe NPDR	191.25	11.537		
	PDR	188.55	14.767		
	Controls	329.18	21.819		
Superior	No Retinopathy	297.00	12.048	147.136	<0.001
	Mild NPDR	267.00	41.204		
	Moderate NPDR	236.59	28.555		
	Severe NPDR	192.83	13.704		
	PDR	191.64	14.144		
	Controls	327.73	18.685		
Inferior	No Retinopathy	293.35	28.673	130.012	<0.001
	Mild NPDR	273.84	46.587		
	Moderate NPDR	236.14	28.501		
	Severe NPDR	200.33	26.898		
	PDR	198.18	59.493		
	Controls	326.45	18.825		
Statistically Significant					

each other, leading co- related complications and outcomes.

The mean age of patients in the study group was 58.86 ±8.034, showing that systemic disorders like diabetes are becoming more common among those age groups. Similar results were observed in a study by wei wang et al., in which they observed a maximum number of patients in the 6th decade. According to various studies, early-onset diabetes is much more aggressive and may be attributed to increased diabetic microvascular damage.[12] The mean duration of diabetes was 5.708 ± 3.906, with the majority of diabetic individuals having a 5-10-year history of the disease. Patients with a longer duration of diabetes were observed to have higher grades of diabetic retinopathy and, subsequently, a lower overall choroidal thickness. Similar observations were also made on evaluating medication history, where the majority of patients (55.2) were on oral medications; however, more severe grades of diabetic retinopathy were noted in patients on insulin therapy (16.5).

Hyperglycaemia is the main initiating component for microvascular alterations and disease progression in

diabetic patients, making it vital to monitor the diabetic status and control of the patient. HbA1c, PPBS and FBS were used to evaluate the diabetic status in the study and control groups. HbA1c levels >8% Were seen in 22 patients with PDR and 21 with severe NPDR. A statistically significant association between higher HbA1c levels and increased severity of retinopathy was noted, which can be attributed to poor diabetic control leading to increased severity in microvascular damage due to hyperglycemia. Similar observations were made on consideration of FBS and PPBS levels.

Until recently, CT insight was primarily based on histologic and histopathology. This, however, did not give necessary measurements of the choroidal. Recent literature has proven the potential of SD-OCT in imaging the choroidal. Manjunath V et al., in their study on CT in normal eyes measured using Cirrus HD optical coherence tomography, demonstrated that CT can be evaluated using SD-OCT.[13]

In our study, the mean CT in controls was 327.308 ± 18.945 microns, with a maximum thickness of 329.18 ± 21.819 microns noted in the temporal area and a minimum thickness of 324.88 ±18.117 microns in the nasal region. Similar results were observed in a study by Entezari M et al. on CT in healthy subjects.[14] The choroidal thickness of diabetes patients without retinopathy had higher CT, with a mean thickness of 295 ± 15.082 microns in comparison to patients with retinopathy. Maximum reduction in CT among patients with retinopathy was observed in patients with PDR, with a mean thickness of 191.492 ± 23.834 microns. Mean CT in the mild NPDR, moderate NPDR, and severe NPDR was 271 ± 36.122, 242 ± 30.048, and 193 ± 15.748 microns, respectively. A statistically significant reduction in mean CT was noted with increasing severity of DR, similar to results by Regatieri CV et al., in which they concluded that, Due to a considerable drop in CT in patients, diabetic choroidal angiopathy was linked to the severity of retinopathy.[15]

5. Conclusion

Choroidal vasculature is essential for the proper functioning of the retina, and deficiencies lead to the dysfunction of photoreceptors. Our study mainly concentrated on the measurement of CT in diabetic patients and was designed as a case-control study for more reliable results. Healthy non-diabetic patients showed a mean choroidal thickness of 327.308 microns, while diabetic patients had an overall thinner CT. An overall reduction in CT was noted with increasing severity, or higher grades of DR. Thinnest choroids were observed in PDR patients with a mean thickness of 193 microns. Thinning of the choroid can be attributed to the hypoperfusion of the choroid due to microvascular changes, eventually leading to choroidal dysfunction. SD-OCT (EDI) proves to be a reliable method to assess choroidal thickness. CT can be used as a non-invasive tool and prognostic marker to aid in the prognosis assessment of DR.

The study's limitations were a lack of patient follow-up and choroidal thickness assessment after diabetic control was achieved in a previously uncontrolled diabetic and an unevaluated macular thickness.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Cite this article: Israel MJ, Ijeri RK, Sankolli NA. Choroidal thickness in type 2 diabetes mellitus patients using spectral domain optical coherence tomography. *Indian J Clin Exp Ophthalmol* 2024;10(3):475-480.