CENTRAL MACULAR THICKNESS IN DIABETIC RETINOPATHY PATIENT WITHOUT CLINICALLY SIGNIFICANT MACULAR EDEMA

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ABSTRACT

Introduction: Diabetic retinopathy is the fifth most common cause of preventable blindness in the world. Clinical features of DR are undetectable at early stages. OCT is rapid, non-invasive, and useful imaging technology for quantitative and qualitative assessment of macula.

Purpose: to describe central macular thickness (CMT) in patient diabetic retinopathy without clinically significant macular edema.

Methods: This is a descriptive study of newly diagnosed patient with diabetic retinopathy from Vitreoretina Unit, Cicendo Eye Hospital National Eye Center between July until September 2019. The patients were performed complete ophthalmology examination, laboratory, and OCT macula.

Results: Twelve eyes from 9 patient were evaluated. The mean age (SD) of the patients was 52,8 (4,9) years. Six from 9 patients were female. All of the patient had DM type 2 with most patient were diagnosed as moderate NPDR. CMT in patient with severe NPDR was 197,5 ± 2,5 and in moderate NPDR was 260,7 ± 14,6. CMT in patient with duration of DM below 5 years was 249,5 ± 1,5, in 5-10 years was 254,3 ± 35,6, and above 10 years was 247,7 ± 24,5. All of the patients had HbA1c above 6,5%.

Conclusion: From this preliminary study with small sample size it seems CMT was thicker in moderate NPDR than severe NPDR without evidence of any clinically significant macular oedema. Patient with duration of DM above 10 years had thinnest CMT. All patient had high HbA1c level.

Keywords: diabetic retinopathy, central macular thickness, optical coherence tomography

INTRODUCTION

Diabetic Retinopathy (DR) is the leading cause of vision loss in adults aged 20–74 years. From 1990–2010, DR ranked as the fifth most common cause of preventable blindness and fifth most common cause of moderate to severe visual impairment. In 2010, of an estimated 285 million people worldwide with diabetes, one-third of diabetic people develop some degree of diabetic retinopathy (DR).[1-4]

Several studies showed that retinal neuronal abnormalities are present at the early stages of DM. These abnormalities as retinal ganglion cell (RGC) death and axonal degeneration should increase with increasing DM duration, and this reduces the RNFL thickness. Ganglion cell-inner plexiform layer (GC-IPL) thickness, a

surrogate measure of neuronal loss, is significantly reduced in persons with diabetes, compared with normal controls. These results strengthen the hypothesis that neuronal degeneration may precede overt vascular changes. Previous studies have also indicated that microaneurysms and other microvascular abnormalities associated with DR are more likely located in the outer retinal layers.[5,6]

Clinical features of DR are undetectable at early stages. Traditional methods for evaluating DR, including slit-lamp biomicroscopy and stereo fundus photography, are relatively insensitive to small pathological changes in the retina. In addition, highly sensitive fluorescein angiography is invasive and not suitable for repeated examination. Optical coherence tomography (OCT) is a rapid, non-invasive, and useful imaging technology for cross-sectional and tomographic imaging in biological tissues, which is especially useful for quantitative and qualitative assessment of macula. Purpose of this study is describe central macular thickness (CMT) in patient diabetic retinopathy without diabetic macular edema.[3,4]

MATERIALS AND METHODS

This is a descriptive study of newly diagnosed patient with diabetic retinopathy from Vitreoretina Unit, Cicendo Eye Hospital National Eye Center between July until September 2019. Patient with diabetes and newly diagnosed DR were enrolled if they met the inclusion criteria.

Inclusion criteria included the following: (1) patients above 18 years old with newly diagnosed as any degree of diabetic retinopathy; (2) Intraocular pressure below 21 mmHg; (3) spectral domain OCT with a signal-to noise ratio of 0.6 or greater. Exclusion criteria included the following: (1) history of trauma within the last 6 months; (2) history of intraocular surgery within the last 6 months; (3) history of used chronic corticosteroid within the last 3 months; (4) patient with optic neuropathy and other retinal disease than DR; (5) patient with clinically significant macular edema; (6) CMT > 300 µm.

Patients‘ baseline characteristics were recorded including age, sex, type and duration of diabetes, glycosylated haemoglobin A1C level (HbA1c), and disease laterality. All patient underwent a complete ophthalmic examination including UCVA (Snellen), intraocular pressure (IOP) using noncontact tonometry, slitlamp biomicroscopy and dilated fundus examination. Central macular thickness measurement was performed with Carl Zeiss Meditec OCT fast macular cube 512x128.

RESULT

Total 12 eyes of 9 patients met all the eligibility criteria. Baseline characteristics are shown in table 2. The mean age (SD) of the patients was 52,8 (4,9) years. Six from 9 patients were female. All of the patient have type 2 diabetes and most of patients were diagnosed as moderate NPDR.

Table 1. Data of Patient

No.	Sex	Age	Duration of DR (years)	Classification of DR	HbA1c	Dyslipidaemia	Hypertension	CMT
1	female	45	3	moderate NPDR	7,5	yes	yes	251
2	female	45	3	moderate NPDR	7,5	yes	yes	248
3	female	57	13	moderate NPDR	7,8	yes	yes	259
4	female	57	13	moderate NPDR	7,8	yes	yes	261
5	female	55	15	moderate NPDR	8,6	yes	no	250
6	female	48	14	moderate NPDR	7,6	yes	no	251
7	male	53	7	moderate NPDR	9,8	yes	no	247
8	male	53	7	moderate NPDR	9,8	yes	no	275
9	male	56	22	moderate NPDR	9,2	yes	yes	270
10	female	61	9	moderate NPDR	10,8	no	no	295
11	male	53	10	severe NPDR	7,5	yes	yes	195
12	female	47	10	severe NPDR	11,5	yes	yes	200

Table 2. Characteristic of Patient

Characteristic	Mean ± SD	n (%)
Sex		
Male		3 (33,3%)
Female		6 (66,7%)
Age	52,8 ± 4,9	
Duration of Diabetes		
< 5 years		2 (16,7%)
5-10 years		5 (41,7%)
> 10 years		5 (41,7%)
Type of diabetes		
Type 1		0
Type 2		12 (100%)
Classification of DR		
Mild NPDR		0
Moderate NPDR		10 (83,3%)
Severe NPDR		2 (16,7%)
PDR		0
HBA1C		8,9 ± 1,4
Laterality		
Unilateral		7 (77,8%)
Bilateral		2 (22,2%)
UCVA		
≤ 3/60		1 (8,3%)
4/60-6/18		6 (50,0%)
> 6/18		5 (41,7%)

DR: diabetic retinopathy
NPDR: non proliferative diabetic retinopathy
PDR: proliferative diabetic retinopathy
HBA1C: glycosylated haemoglobin A1C
UCVA: uncorrected visual acuity

Table 3 show mean central macular thickness in moderate NPDR was 271,6 ± 38,5, severe NPDR was 197,5 ± 2,5, and PDR was 382 ± 40,2.

Table 3. Central Macular Thickness and Degree of DR

Degree of DR	CMT (Mean ± SD)
Moderate NPDR	260,7 ± 14,6
Severe NPDR	197,5 ± 2,5

Table 4 show mean central macular thickness in patient with < 5 years duration of diabetes was 249,5 ± 1,5, in 5-10 years was 254,3 ± 35,6, and in > 10 years was 247,7 ± 24,5.

Table 4. Central Macular Thickness and Duration of DM

Duration of Diabetes	CMT(mean ± SD)
< 5 years	249,5 ± 1,5
5-10 years	254,3 ± 35,6
> 10 years	247,7 ± 24,5

Table 5 show patient with HbA1c level between 7-9% had CMT 245 ± 20,9 and patient with HbA1c level >9% had CMT 257,4 ± 32,5.

Table 5. Central Macular Thickness and HbA1c level

HbA1c level	CMT (mean ± SD)
<7,0%	0
7,0-9,0%	245 ± 20,9
>9,0%	257,4 ± 32,5

DISCUSSION

The leakage and collection of lipid exudates within the retinal layers leads to macular oedema. This is a major cause of decreased vision in Diabetic Retinopathy. Hence, assessment of thickness of central macula is important. OCT is used to quantitatively measure macular thickness for diagnosis and management of macular oedema and also to detect subclinical macular thickening in diabetic retinopathy.[9,-11]

Oshitari et al reported that in early stage of diabetic retinopathy central macula was significantly thinner than controls. This was explained by the neuronal abnormalities due to diabetes including retinal ganglion cell death and axonal degeneration. These neuronal alterations were hypothesised to precede the vascular abnormalities in diabetic subjects with early diabetes and thus were responsible for thinner macula in diabetic patients. On comparing mean CMT in different DR subgroups, it was found to be progressively increasing with increasing stage of DR. This increased macular thickness with progressively increasing retinopathy can be explained by alterations in vascular permeability of peri-foveal and macular capillaries in diabetics eyes.[3,4]

Previous study suggests that changes in macular thickness can be detected by OCT despite normal findings in funduscopy. These patients are candidates for more frequent and more detailed follow up as they are likely to develop CSME. Previous studies have reported that several risk factors, including HbA1c level, duration of diabetes, hypertension, hyperlipidaemia, body mass index (BMI), sex, and insulin treatment, are involved in the development of DR and thickening of macula and outer retina.[4,6]

In our study seems that central macular thickness in severe NPDR group was thinner than moderate NPDR. It was different with previous study that explained CMT will progressively increase concomitant with stage of DR. Only 2 cases diagnosed as severe NPDR, one of them had atrophy macula.[8,9]

In table 4 show 5-10 years duration of DR had a little bit thicker CMT than other groups. In previous study explained that CMT will increase concomitant with duration of DM. It can be explained that CMT is also influenced by controlling of diabetes and other systemic condition such as dyslipidaemia and hypertension. We can see the controlling of diabetic from

HbA1c level in our patient was high with mean 8,9 ± 1,4. Most patient had another systemic condition such as dyslipidaemia and or hypertension. Jiang et al report the same result from their study. The reasons for this result may be that the course time provided by patients was the duration confirmed by diagnostic examination, which was often shorter than the actual duration of illness, and the so-called "course of diabetes" may not have been sufficient to lead to significative retinal structure damage.[3,4]

HbA1c levels predict the incidence and progression of DR. Retinal thickness is inversely correlated with HbA1c levels. Another study has shown that a decrease in HbA1c is associated with thickening of inner retinal layers in the parafovea after bariatric surgery, which dramatically improves the metabolic profile in diabetes. Hypoxic apoptosis of ganglion and axonal cells caused by the high affinity of HbA1c on oxygen (most oxygen molecule integrated with the elevated level of HbA1c instead of ganglion and axonal cells, which lead to the latter hypoxia) may be the most important underlying pathological mechanism. In this study, all patient had HbA1c level >7,0%. The reason is because Cicendo eye hospital is national referral centre, patient who came with severe degree of disease. Murugesan et al reported no relationship between the HbA1c level and the CMT.[3,8]

Central macular thickness can be associated with decrease in visual acuity. Visual acuity in diabetic patients not only depends on oedema formation but also on capillary destruction in the macula. Vujosevic reported there is significantly correlation between visual acuity and CMT in the NCSME (no clinically significant macular edema), but not in the NE (no edema) or in the CSME. American Academy of Ophthalmology reported in their study there was many eyes with a thickened macula had excellent visual acuity, and many eyes with a macula of normal thickness had decreased visual acuity. These results suggest that visual acuity alone is not a reliable surrogate measure for the retinal thickness evaluation.[12-14]

Limitation of this study are the short period of the data collection, in homogenous total sample in each group and small number of sample. Further study included comparison of CMT in healthy control group and no DR group with larger sample size.

CONCLUSION

This was a preliminary study with small sample size, it seems CMT was thicker in moderate NPDR than severe NPDR without evidence of any clinically significant macular oedema. Patient with duration of DM above 10 years had thinnest CMT. All patient had high HbA1c level. OCT is a promising diagnostic tool for detection early stage of diabetic retinopathy.

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