Comparison of Central Macular Thickness between Diabetic Patients without Clinical Retinopathy and Non-diabetic Patients

Upasana Pokhrel[1], Eli Pradhan[2], Rabindra Singh Thakuri[3], Kaushal Pokhrel[4], Govinda Paudyal[2]

[1]B.P. Koirala Institute of Health Sciences, Dharan, Nepal
[2]Tilganga Institute of Ophthalmology, Gaushala, Kathmandu, Nepal
[3]Bharatpur Eye Hospital, Bharatpur, Nepal
[4]ASG Eye Hospital, Kathmandu, Nepal

ABSTRACT

Introduction: Diabetic retinopathy (DR) is one of the leading causes of blindness in patients between 20 and 60 years of age which can be prevented by early detection of diabetic retinopathy. The duration of diabetes is probably the strongest predictor for development and progression of retinopathy. Optical Coherence Tomography (OCT) is a recent advance in imaging which is sensitive in early detection of small changes in macular thickness.

Materials and Methods: This hospital based cross-sectional study was done at a tertiary referral center in Kathmandu, Nepal where 364 eyes of 182 patients (182 eyes in 91 patients in each group diabetes without retinopathy group and nondiabetic group) were evaluated. Thickness of the macula was determined by using Spectral Domain Optical Coherence Tomography (SD- OCT) and compared between diabetic patients without clinical retinopathy and nondiabetic patients.

Results: The mean CMT as measured by Spectral Domain Optical Coherence Tomography in diabetic patients was 236.29±40.31 µm whereas it was 244.25±30.51 µm in non-diabetic cases. The mean central macular thickness of diabetic patients with duration of diabetes less than 1 year, 1-5 years, 6-10 years, 11-15 years and more than 15 years were 217.19±42.22, 233.49±45.69, 248.5±31.37, 250.89±21.62 and 240.75±11.26 respectively.

Conclusions: This study concluded that in diabetic patients there was an initial decrease in central macular thickness which gradually increased with increasing duration of diabetes mellitus. Examination of macular thickness could be a useful modality to evaluate progression of disease before appearance of other clinical signs of diabetic retinopathy.

Key words: Diabetic retinopathy, Early diagnosis, Optical Coherence, Tomography.

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Corresponding Author
Dr. Upasana Pokhrel
Patan Academy of Health Sciences,
Lalitpur, Nepal.
E-mail: upasanapokhrel@gmail.com

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INTRODUCTION

Diabetic retinopathy (DR) is an important cause of blindness that affects diabetic patients, especially between the age of 20 and 60 years. (Biallosterski et al., 2007) It is important to identify the DR early to prevent the loss of vision because the duration of diabetes is one of the biggest predictors of the development and progression of retinopathy.

The macular thickness is increased in many retinal conditions including diabetic retinopathy, age-related maculopathy, central serous chorioretinopathy, and venous occlusions. (Verma et al., 2009) Measurement of macular thickness is an important tool for evaluation of the disease and its progression. The different methods used for evaluation of macula include direct and indirect ophthalmoscopy, slit-lamp biomicroscopy, fundus photography, fluorescein angiography and optical coherence tomography. (Pokharel et al., 2016)

Of different techniques for evaluation of macula, Fluorescein angiography (FA) is more sensitive than slit-lamp biomicroscopy for the qualitative detection of macular edema. However, invasiveness of the former with a number of side effects, is expensive and time consuming. Furthermore, it is a qualitative tool and cannot quantitatively assess the macular thickness.

Optical coherence tomography (OCT) , which has changed the way we see and evaluate the retina, can perform micrometer resolution cross-sectional or tomographic imaging in biologic tissues. The principle of OCT is based on low-coherence interferometry. OCT requires no contact, is non-invasive, rapid and more accurate to detect early macular thickening compared with other methods used for evaluation of macular thickness.(Pokharel et al., 2016)

OCT has been used for diagnosis and evaluation of different conditions involving anterior segment and retina in patients with selected macular abnormalities and glaucoma. In diabetic patients it can help in evaluation of macular edema and central foveal thickness. In patients with diabetes and no clinical signs of retinopathy, different studies have reported that there is a decrease in Retinal Nerve Fibre Layer (RNFL) thickness in the macula. One possible explanation for the above finding may be the progressive ganglion cells and astrocytes loss induced by hyperglycemia.(Vujosevic and Midena, 2013) Early detection of macular changes in diabetic patients is particularly essential because advanced DR is more refractory to treatment. OCT might be valuable tool due to its sensitivity to detect much earlier signs and structural macular changes compared to funduscopic or photographic examinations. (Sugimoto et al., 2005) (Lattanzio et al., 2002) Shallow changes in retinal thickening of less than 100 microns may be invisible during slit lamp biomicroscopy and ophthalmoscopy but, it is easily observed in OCT.(Lattanzio et al., 2002) OCT is also helpful in follow up and treatment of diabetic retinopathy and monitoring therapeutic response by evaluating macular thickening before and after laser therapy. It is highly sensitive for demonstration of areas of subclinical macular edema, as well as to confirm the presence or absence of macular thickening. (Salz and Witkin, 2015) The use of OCT may quantify macular edema with macular thickness and decrease the risk of laser-induced paracentral scotomas in cases

with clinically suspicious macular edema. (Browning et al., 2004) In patients without other macular abnormalities, loss of different retinal layers can be visualized which can explain the loss of vision and functional abnormalities such as chromatic discrimination and contrast sensitivity.(Lieth et al., 2000; Salz and Witkin, 2015; Simó et al., 2012; Zhu et al., 2015).

The proposed mechanisms of apoptosis of retinal ganglionic cells are neurofilament accumulation related to changes in retrograde axonal transport; elevated levels of glutamate; increasing neurotoxic factors and reactive changes in microglia.(Carpineto et al., 2016) By measuring thickness changes in the inner retinal layers in the ETDRS areas especially in the ganglion cell bodies located in ganglionic cell layer at parafoveal level OCT can be helpful to develop a possible strategy to slow DR.(Carpineto et al., 2016; Orduna-Hospital et al., 2021; Pinilla et al., 2020; Sohn et al., 2016)

In developing countries like Nepal, patients usually present late in the course of DR, mainly due to lack of awareness. Early detection of macular changes in eyes of diabetic patients before other clinical signs of retinopathy would thus be valuable in initiating early treatment of DR. This study aims to evaluate early macular changes in patients with diabetes having no clinical diabetic retinopathy by comparing macular thickness with non-diabetic patients and to compare the change macular thickness in diabetic patients according to duration of diabetes.

MATERIALS AND METHODS

This hospital based cross-sectional study was conducted in a tertiary eye hospital in Kathmandu, Nepal after ethical clearance from the Institutional Review Board (IRB). The sample size of our study was calculated as 91 in each group after considering the prevalence of diabetes in Nepal of 6.3% (Sharma et al., 2011), precision of 5% and confidence interval of 95%. Ninety-one consecutive patients with diabetes without clinical diabetic retinopathy who met the inclusion criteria were taken. The control group consisted of 91 consecutive non diabetic patients without any history of random sugar levels more than 200. Informed written consent was taken from all included patients in the study.

Patients included were diabetic patients without diabetic retinopathy, maculopathy or papillopathy . Non diabetic patients without macular abnormalities were included as a control group. In both these groups corrected distant visual acuity was 6/9 or better.

Patients with Ocular pathologies which obscure fundus evaluation, with prior treatment with LASER or intra-vitreal anti-VEGF injections and history of intraocular trauma or surgery were excluded from the study.

Detailed history was taken from the patients. Visual acuity was taken with the standard ETDRS (Early Treatment Diabetes Retinopathy Study) visual acuity chart at 4m. Detailed anterior segment examination was done under a slit-lamp biomicroscope. Posterior segment examination was done with the help of 90D lens under mydriasis and was checked for status of vitreous, optic disc, macula and peripheral retina. Central macular thickness of all included patients was measured using SD OCT.

Statistical analysis was performed with statistical software (SPSS 25.0 for Windows). Statistical tests of significance used were Chi-square (χ^2) test, independent sample t-test and one-way ANOVA. P-value was calculated under the predetermined level of significance (0.05).

RESULTS

Of 182 patients enrolled in the study, there were 41 males and 50 females in the diabetic group and 30 males and 61 females in the nondiabetic group. The patients were aged between 30 to 74 years (mean age 48.8± 9.74 years). The mean age (51.87± 9.92) of patients with diabetes was higher (p value <0.001) than of those without diabetes (45.85± 8.6 years). The mean duration of diabetes among 91 diabetic patients was 5.4± 4.7 years of which 16 cases were newly diagnosed, 40 cases had disease for 1-5 years, 22 for 6-10 years, 9 for 11-15 years and 5 had diabetes for more than 15 years. Thickness of the macula was determined by using Spectral Domain Optical Coherence Tomography (SD-OCT) as depicted in Figure 1.

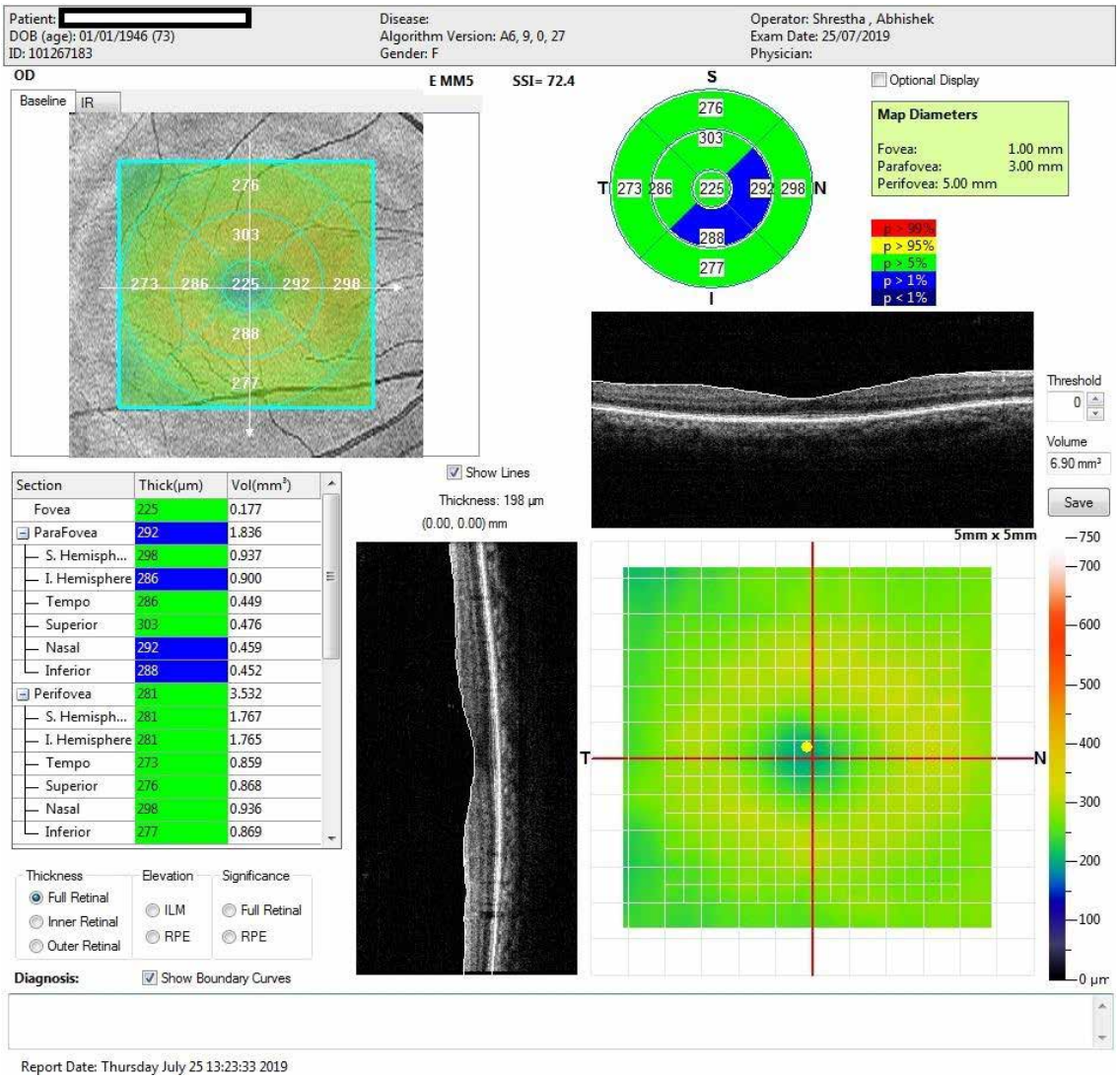

Figure 1: Measurement of central macular thickness by SD OCT.

Table 1: Central macular thickness in relation to duration of diabetes.

Duration of Diabetes (in years)	Number of patients	Mean central macular thickness (µm) (±SD)	P- value
<1	16	217.19±42.22	<0.001 (one way ANOVA)
1-5	40	233.49±45.69	
6-10	22	248.5±31.37	
11-15	9	250.89±21.62	
>15	4	240.75±11.26	
Total	91	236.29±40.31	

In table 1 we compared the mean central macular thickness in different age groups according to the duration of diabetes. Central macular thickness was found to increase significantly in diabetic patients with increased duration of diabetes.

In figure 2 we compared the mean CMT in different age groups in diabetic and non-diabetic patients. The mean CMT was 237±24.1, 232.38±41.59, 231.62 ±43.44, 251.5±42.03 and 251.5±18.42 µm in the age group 30 to 40, 41 to 50, 51 to 60, 61 to 70 and more than 70 years respectively in cases having diabetes mellitus while the mean CMT was 243.93±31.28, 241.96±31.28, 248±33.32, 251.9±41.65 and 244.5 ±2.12µm in the age group 30 to 40, 41 to 50, 51 to 60, 61 to 70 and more than 70 years respectively in cases without diabetes mellitus.

The mean CMT as measured by SD-OCT in diabetic cases and non-diabetic cases were 236.29±40.31 and 244.25±30.51 µm respectively as depicted in table 2. Diabetic patients had significantly lesser central macular thickness compared with nondiabetic patients.

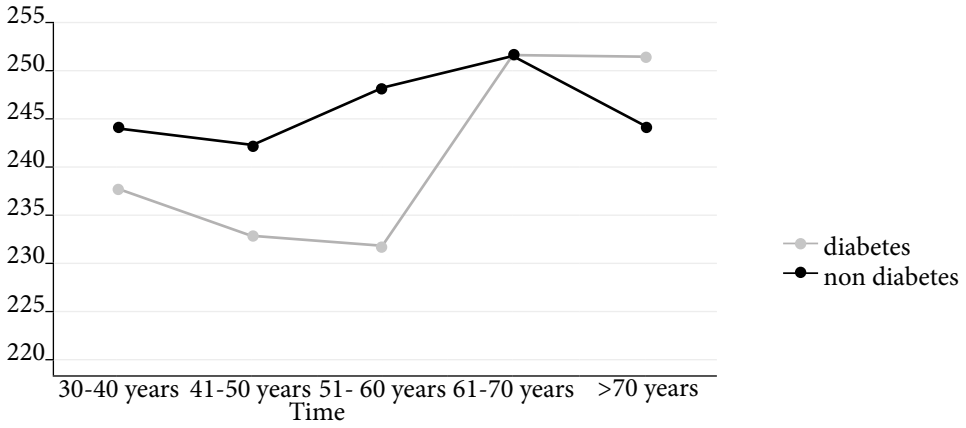

Figure 2: Mean central macular thickness in different age groups.

Table 2: Mean Central macular thickness in both groups.

	Number of patients	Number of eyes checked	Central macular thickness(µm) (±SD)	P value
Diabetic	91	182	236.29±40.31	0.034 (independent t test)
Non diabetic	91	182	244.25±30.51	

DISCUSSION

This was a hospital based cross sectional study where we compared the central macular thickness of 182 eyes in 91 consecutive patients with diabetes mellitus without clinical retinopathy with an equal number in patients without diabetes. In our study, the mean age of the patient with diabetes without retinopathy was slightly higher than nondiabetic patients which is comparable to other studies. (Verma et al., 2009), (Demir et al., 2013). Most of the diabetic patients in the study had duration of diabetes less than 5 years.

Patients with shorter duration of diabetes had lesser central macular thickness. In patients with duration of diabetes less than 1 year the mean CMT was 217.19±42.22 and in 1-5 years it was 233.49±45.69. This early reduction of macular thickness is probably explained by neuronal degeneration which occurs early in diabetes. As the duration of diabetes increased there was an increase in mean central macular thickness. With increase in duration of diabetes the decrease in macular thickness due to neuronal degeneration is masked by increase in macular thickness associated with vascular leakage which follows the degeneration leading to overall increase in central macular thickness. (Verma et al., 2009) This was supported by Asefzadeh et al who suggested that the macular thickness decreases in early diabetes due to neural tissue loss. However, with progression of diabetes and increase in vascular permeability central macular thickness gradually increases. (Asefzadeh et al., 2008; Chen et al., 2016; Oshitari et al., 2009)

Dumitrescu AG et al,(Dumitrescu et al., 2017) did a similar study in patients with type 2 diabetes mellitus where central macular thickness was significantly thinner than that of control eyes. Sanchez-tocino H et al,(Sánchez-Tocino et al., 2002) concluded that their study fully supported previous suggestions that early changes in retinal thickness could be detected by OCT despite normal findings in slit lamp biomicroscopy. Van Dijk HW et al, (van Dijk et al., 2009) and Park et al,(Park et al., 2011) suggested that early neuronal loss occurs in DR that results in selective thinning of inner retinal layers in the central retina leading to thinning of the total retina in diabetic patients with minimal retinopathy.

The central macular thickness in diabetic cases without retinopathy in our study was 236.29±40.31 µm which was significantly lesser than the central macular thickness in non-diabetic cases which was 244.25±30.51 µm. This is explained by more number of patients in the diabetic group who had duration of diabetes less than 5 years which had initial reduction in central macular thickness due to neuronal degeneration.

Strengths of the study

Adequate sample size of 182 eyes in 91 patients each study group was evaluated in the study. Standardized method of measurement of macular thickness by SD OCT was used. Statistically significant difference was found in macular thickness in diabetic and non-diabetic patients and according to increase in duration of diabetes in diabetic patients.

CONCLUSION

In diabetic patients there was an initial decrease in central macular thickness due to neurodegeneration which gradually increased with increase in vascular permeability with increasing duration of diabetes mellitus. Examination of macular thickness could be a useful modality to evaluate progression of disease before appearance of other clinical signs of diabetic retinopathy.

LIMITATIONS

Our study was a cross sectional study. The change in macular thickness in diabetic patients over time could be evaluated better by a prospective study design. We studied changes in central macular thickness only. Thickness changes in other macular quadrants could be evaluated in more extensive study. Other more sensitive techniques such as 3D OCT could be used to determine whether similar differences can be found.

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