ISSN: 0975 -8542

Journal of Global Pharma Technology

Available Online at: www.jgpt.co.in

RESEARCH ARTICLE

The Comparison of Macular Thickness in Diabetic Patients without Proliferative Diabetic Retinopathy using Optical Coherence Tomography (OCT) at Prof. Dr. R D Kandou General Hospital, Manado, Indonesia

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Abstract

Background: Macular thickening that occurs in diabetic retinopathy has been known as one of the primary causes of vision loss functions in patients with diabetic retinopathy. In order to prevent further complications due to macular thickening, Optical Coherence Tomography (OCT) has been used as a diagnostic tool in diabetic retinopathy. This study aims to evaluate the importance of OCT in promoting early detection in retinal thickening as diagnostic tools and proper exams to diminish the chance of visual acuity related to diabetic retinopathy. Method: A case-control observational study was conducted among 22 subjects with Diabetes Mellitus Type-2 (DM-2) from the medical record of the Ophthalmology-Vitreoretinal Division at Prof. dr. R.D. Kandou State General Hospital, Manado from March-December 2018 period. They were divided into 11 patients with mild and moderate non–proliferative diabetic retinopathy (NPDR) and 11 non-diabetic patients' group. OCT was used to evaluate the macular thickness in both groups. Data were analyzed using SPSS version 20 for Windows. Result: Most of subjects were female (59.1%), age 45-50 years (31.8%), ≥ 10 years duration of DM-2 (63.6%), refractive errors of 0.00-(-3.00) and 0.00-(+3.00) (33.3%), and HbA1c levels ≥6.5 % (54.5%). There was a statistically significant difference of the central macular thickness between NPDR (257.32±76.94 µm) and non-NPDR patients (213.14±19.23 µm) (p=0.006) by using OCT. Conclusion: Optical Coherence Tomography (OCT) could be used to compare the significant differences of macular thickness between diabetic patients without proliferative diabetic retinopathy at Prof. Dr. R D Kandou General Hospital, Manado, Indonesia.

Keywords: *Macular Thickness, Diabetic Retinopathy, Optical Coherence Tomography*.

Introduction

Diabetes mellitus is a global health issue affecting all ages [1]. With the increase in the number of diabetes mellitus disease patients, one of the foremost complications, diabetic retinopathy is found proliferated and is considered as one of the prominent causes of vision loss globally [1, 2].The prevalence of diabetes mellitus in 2010 reached 6.4% of the world's population or in an approximate of 285 million individuals [1]. This phenomenon is estimated to increase for up to 7.7% or 440 million individuals by 2030 [1].

In Indonesia, diabetes mellitus prevalence has been reported to have experienced an increase of 5.6% in 2013 and is estimated to amount to 6.7 by 2035 [2]. The prevalence of diabetes mellitus in the province of North Sulawesi is 6.1% higher than the prevalence of national diabetes mellitus.2 Furthermore, individuals who carry type 1 (DM-1) and 2 (DM-2) diabetes mellitus are more likely to have diabetic retinopathy [3]. In Indonesia, around 17.2-42.6 % of individuals are known with diabetic retinopathy [3]. Other studies found that individuals with DM-1 have a prevalence of 35.7 % diabetes retinopathy, while individuals with DM-2 experience a slightly higher percentage, at 40% of diabetic retinopathy due to several factors [4, 5].

Upon the publication of this study, there is no report on the national burden about diabetic retinopathy, except the visual loss caused by diabetic retinopathy affects the severity of mortality rates [6]. With diabetes mellitus being the most common energy metabolism disorders, various micro vascular

complications can be adapted [5, 6].These disorders can affect small blood vessels, including nephropathy, neuropathy, and microangiopathy in which later can occur in the blood vessels of the eye [6].

Moreover, in the area where the damage to blood vessels takes effect, hyper permeability and leakage of micro aneurysms lead to fluid cumulation [6]. In non-perfused areas, retinal thickening can occur in response to ischemia without blood vessel leakage through the mechanism of hyper capillary permeability [7]. The macula is a part of the retina that is very sensitive to light and plays an important role in central human vision. Macular thickening that occurs in diabetic retinopathy is one of the causes of vision loss functions in patients with diabetic retinopathy [7]. Early diagnosis and prompt treatment are the two crucial factors determining the prognosis of visual functions in diabetic patients.

Histological Examination with Hematoxylin and Eosin (H&E) staining on the retinal section can initially be used to measure macular thickening. However, this approach is unable to be conducted on a living human since it will require the retina to be incised and then checked under a microscope [8].Thus to this day, the conventional time-domain Optical Coherence Tomography (OCT) exams have been used in many studies and played an important role of a diagnostic tool in assessing macular thickness [7, 8].

This study chooses to measure macular thickness using OCT because it is a non-invasive approach which uses low coherent light near that of the infrared to create a cross-sectional image of the retina and is believed to provide a better understanding in quantifying responses to assessing various visual implications triggered by macular thickness. OCT, just like Ultrasonography, works by using sound waves.

However, the only difference is OCT uses light to create a cross-sectional image of the retina [9].Today; OCT is one of the imaging modalities for the diagnosis of diabetic retinopathy [10]. Based on those mentioned above, this study aims to evaluate the macular thickness among diabetic patients with NPDR using Optical Coherence Tomography (OCT) at Prof. Dr. R D Kandou General Hospital, Manado, Indonesia.

Methods

This study is a case-control observational study undertaken in the medical record of the Ophthalmology Division, Vitreoretinal Division in Prof. dr. R.D. Kandou State General Hospital, Manado from 1st March 2018 to 31st December 2018. Eleven subjects with mild and moderate NPDR and eleven of non-NPDR with normal blood sugar levels and no found retinopathy signs were recruited for this study.

Optical Coherence Tomography was acquired and performed by an appointed physician in a stated hospital. The inclusion criteria for this study were the age of 40 and over and those of the NPDR group with mild to moderate grades who had a 6/6 vision either with or without correction and had had OCT data. On the other hand, non- NPDR groups were those who came to undergo regular checkups of ophthalmic examinations with none retinal abnormalities, showed normal blood sugar and HBa1c levels.

Both groups further underwent retinal fixation in the fovea on the OCT examination. All the eligible subjects were then inquired to sign informed consent regarding the confidentiality used in this research. Exclusion criteria were the other systemic abnormalities found during the study, such as hypertension and blood clotting anomaly, retinal aberrations other than NPDR. NIDEK RS 3000 OCT scan was used for the macular thickness analysis among 44 eligible-eyes.

The data obtained from the OCT machine were documented in the medical record and then transferred to the table list used in this study. The posterior segment was examined using direct ophthalmoscopy to match the subject to one of the research groups. Both subject groups were allocated in front of the OCT machine and had their chin on the chin rest, which then had their eyes carefully examined.

After the triage, OCT fast macular scans were obtained from both groups. The results of the OCT imaging scans were then processed by the computer to find out the average mean of macular thickness. Mann-Whitney test was applied to compare the mean of two groups with a 95% confidence interval due to data were not normally distributed in this study.

The subjects' characteristics were reported in the frequency distribution table. Data were analyzed using SPSS version 20 for Windows.

Results

According to gender, this study found that the proportion of females (59.1%) was higher compared with male (40.9%) subjects. Most of subjects were in the 45-50 age-group (31.8%), following by ≥10 years duration of DM-2 (63.6%), refractive errors of 0.00-(-3.00) and 0.00-(+3.00) (33.3%), and HbA1c levels ≥6.5% (54.5%) (Table 1).

Table 1: Baseline characteristic of subjects

Variables	Frequency (N=22)	
	N	%
Gender		
Male	9	40.9
Female	13	59.1
Age (Years)		
45-50	7	31.8
51-55	5	22.7
56-60	4	18.2
61-65	4	18.2
66-70	2	9.1
Diabetes duration		
≥10 years	14	63,6
<10 years	8	36,4
Refractive errors		
≥-3.00	3	6.7
0,00 - 3.00	15	33.3
no refractive errors	12	26.7
0.00 - +3.00	15	33.3
HbA1c levels		
<6.5%	10	45.5
≥6.5%	12	54.5

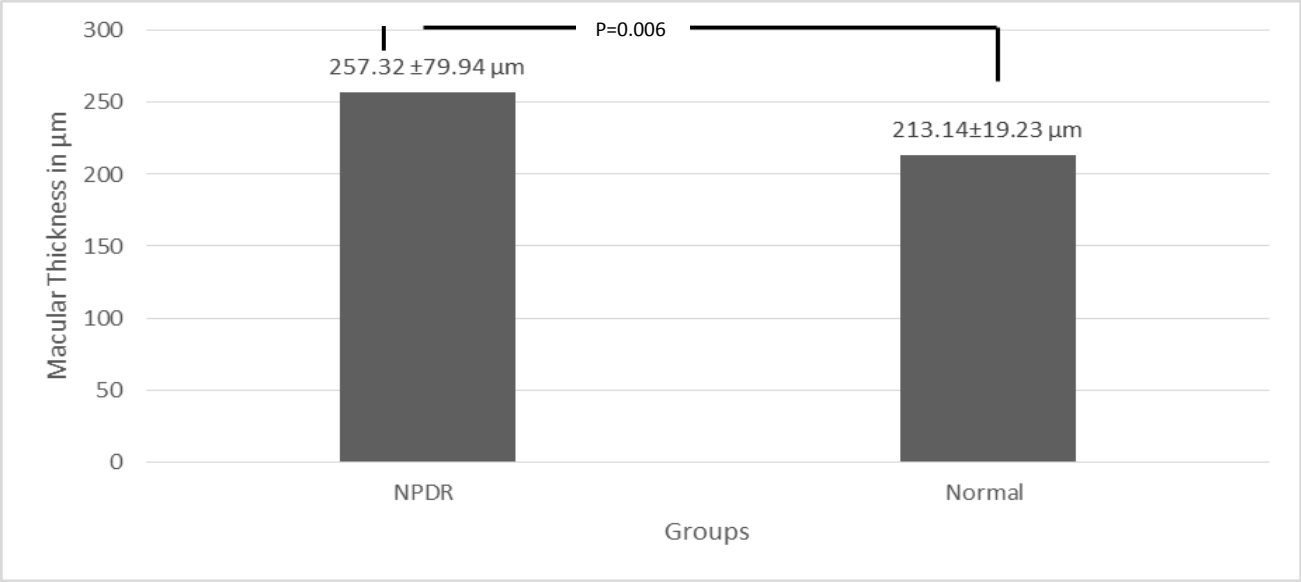

Figure 3: The macular thickness comparison among the two groups by OCT device

In Figure 3, the comparison of the macular thickness measurements obtained from two eligible subject groups, NPDR and non-NPDR patients. There was a statistically significantly different in the mean of macular thickness in the NPDR group (257.32±76.94

μm) compared with the non-NPDR group (213.14±19.23 μm) by Mann-Whitney test (p=0.006) (Figure 1).

Discussion

Due to diabetic retinopathy (DR) becoming a common complication, early detection is in retinal thickening is considered crucial to reducing the incidence of vision loss. In this study, the authors compared the measurement of mean macular thickness using Optical Coherence Tomography (OCT) found in both females and males with both NPDR and non-NPDR.

It is found that macular thickness in NPDR subjects with 6/6 visual acuity was significantly thicker than the non–NPDR subjects. In addition, there have been several studies that were done globally that's express controversial findings regarding the role of gender as one of the factors in the prevalence of DM-2, which further developed to diabetic retinopathy. In 2016, Prof. Dr. R.D Kandou General Hospital diagnosed 55.1% of females had diabetic retinopathy compare to men [11].

Similarly, a study by Kawasaki R et al., also discovered that females showed a more significant percentage of diabetes retinopathy than men [12]. This study was then supported by a study of Melo LGN et al., which found that 55.8% of females had diabetic retinopathy compared to men [4].

Cherci S et al., did the study where she was found that males had a higher prevalence of diabetic retinopathy than women [13].Unfortunately, there has not been any research contributing to underlining the pathophysiological explanation in gender susceptibility of diabetic retinopathy despite the significant differences.

Furthermore, our study found that the diabetes duration in NPDR Group subjects, mostly 10 years or more were 63.6% compared with less than 10 years (36.4%). According to The Wisconsin Epidemiologic Study of Diabetic Retinopathy, the prevalence of diabetic retinopathy varied from 28.8% in persons who had diabetes for less than five years to 77.8% in persons who had diabetes for 15 or more years [14]. Increasing duration of diabetes was strongly associated with the presence of DR. There are 7.90-fold and 20.60-fold increased odds of any DR with diabetes with 10 to more than 20 years' duration compared to less than 10 years' continuation [15].Accordingly, HbA1c 6.5% or above was found in 12 subjects. HbA1c is a useful biomarker of long-term glycemic control [16]. The American Diabetic Association (ADA) has recommended an HbA1c value of ≥6.5% for diagnosing diabetes [17].

Research from the META-EYE study Group found that there were three significant risks for diabetic retinopathy in diabetes patients, which are Diabetic duration, HbA1c, and blood pressure [18]. Therefore, patients with high HbA1c level should be checked for the possibility of diabetic retinopathy occurrences. Furthermore, other studies conducted by Hee M et al., Fritsche P et al., and Massin P et al., found that macular thickness was thicker in the diabetes retinopathy group compared to non-diabetes retinopathy group.[19-21]

Hee M et al. found that an average macular thickness was 179±17 μm in diabetes retinopathy group and 174±21μm in the normal group [19]. Meanwhile, Fritsche P et al. found 181±26 and 152±15 μm in diabetic retinopathy and normal subjects, respectively [20]. Massin P et al. found 174±19 in the Diabetic retinopathy group and 170±18 in the normal group [21]. Therefore, it is clear that people with diabetic retinopathy are more likely to have macular thickness compared with normal subjects. On the other hand, this study has potential limitations.

The calculation of the macular thickness depended on the OCT's database, which then is subjected to biases due to the racial differences between the database population and the research demography. For instance, Chan A et al., in the New England Eye Center found that the average macular thickness in the normal population was 212 ± 20 micrometers [22].

In the same study report, Chan A et al., reported several other studies from 1995 to 2004 that indicated the macular thickness of normal people averaging under 200 micrometers [22]. Perhaps this is due to racial differences that occur at different research sites as it is known that racial differences show differences in retinal thickness [23-25].We estimate that there are particular differences between the average

retinal between ethnic groups in Indonesia. Consequently, further research about these differences is expected. This study only focused on the macular thickness and limited diabetes profile, blood pressure, and lipid status was not collected. Popular pathophysiology features about diabetic retinopathy such as advanced glycation end products (AGEs), Protein kinase C (PKC) were not yet covered in this research either. Further research needs to elaborate on them in order to overcome this study limitation.

Conclusion

In conclusion, macular thickness in NPDR subjects with 6/6 visual acuity was thicker than the normal populations. These findings indicate that there has been an anatomical change in the retina in patients with diabetes mellitus, even in the absence of blurred vision. Therefore, this study believes that with the help of Optical Coherence Tomography (OCT) examination in detecting macular abnormalities in both individuals with and without diabetes retinopathy, it can promote more awareness of factors correlates with visual acuity.

Ethical Clearance

Prof Dr. R. D Kandou General State Hospital Ethical Committee approved this research. Ethical clearance was approved and guaranteed prior to the study was conducted by a number of 239/EC-KEPK/XI/2018.

Author Contribution

Both authors are equally contribute in this study from the conceptual framework, data gathering, data analysis until reporting the results of study through publication.

Acknowledgment

The authors would like to thank Otilia Vanny Rembaen for her assistance and contribution as a language advisor in the preparation of this manuscript.

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