Retinal Nerve Fiber Layer Thickness and Optic Nerve Head Parameters in Open Angle Glaucoma With Diabetes Mellitus Type 2

Masitha Dewi Sari, Soraya Fasya, Aslim D Sihotang

Department of Ophthalmology, University Of North Sumatra

***Abstract*- Background :** Glaucoma is the second leading caused of blindness in the world. Diabetes Mellitus is an independent risk factor in open angle glaucoma.. Among those who have suffered DM will have impact on vascular autoregulation disturbance that small vessel involvement may cause the retina and optic nerve become more susceptible to pressure related damage

Aim : To identify the Retinal Nerve Fiber Layer (RNFL) thickness and optic nerve head parameters in open angle glaucoma patients with diabetic mellitus type 2 in Adam Malik Hospital.

Methods : A prospective, analytical observational with cross sectional methods was conducted at the Adam Malik Hospital from September 2014 to Mei 2014 after approved by the Ethics Committee for Health Research University of North Sumatera School of Medicine.. Thirty four open angle glaucoma patient with diabetus mellitus type 2 and thirty four patients primary open angle glaucomas as a control with age-matched subjects underwent a complete ophthalmological examination and imaging with Cirrus HD-OCT for the evaluation RNFL and optic nerve head.

Result : Superior RNFL was statically significant thinner in diabetic group (P=0,019[8]) compared to the control group. There was no significant difference in temporal-nasal-inferior and average RNFL and there was no significant differences in parameters of optic nerve head

Conclusion : The existence of diabetes should be seriously considered in evaluating the result of RNFL and optic nerve head by imaging.

***Index Terms*-** Open Angle Glaucoma, Diabetes Mellitus, RNFL

I. Introduction

Diabetic is a complex disease resuting from the inability of the body to produce insulin, a hormone that takes sugar out of the blood and into cells where it can be used for energy. Diabetes most common in adult-onset diabetes. Adult-onset diabetes typically strikes those who are over 40, a family history of diabetes and certain ethnic groups[1,2,3] .In Indonesia, there were 9 million cases of diabetes in 2008[4].

Glaucoma refers to a group of diseases that have common a characteristic progressive optic neuropathy with associated with visual function loss and higher of intraocular pressure as a risk factor[5,6]. Open Angle Glaucoma (OAG) is characterized as a chronic, slowly progressive, optic neuropathy with characteristic patterns of optic nerve damage and visual field loss. Elevated IOP, advanced age, positive family history, myopia and Diabetes mellitus have contribute to the risk of developing this disease[7,8].

Several large epidemiological studies have reported positive associations between diabetes and open angle glaucoma. Glaucoma occurs more often in patients with diabetes (5%) than in the general population (2%)[9]. There are clear biologically plausible mechanisms supporting an association between diabetes and OAG. Microvascular damage from diabetes could impair blood flow to anterior optic nerve, resulting in optic nerve damge and diabetes also impairs the autoregulation of posterior ciliary circulation, which may exacerbate glaucomatous optic neuropathy. Finally, individuals with diabetes may be vulnerable to elevated intraocular pressure with more severe visual field loss[9,10,11,12].

Evaluation of the retinal nerve fiber layer (RNFL), as a means of assessing optic nerve health, has been a well-established clinical and investigational tool. Recent studies have supported the finding that diabetes mellitus was associated with thinning of RNFL[13,14]

The aim of our study was to determine that diabetes mellitus type 2 was associated with thinning of RNFL. Patients with the disease were compared to primary open angle glaucoma with no DM as a control subjects of the same aged and sex. .RNFLthickness and optic nerve head enlargement was measured by Cirrus Ocular Tomographhy (Cirrus HD-OCT).

II. Subjects and Methods

Subjects

This was a prospective, noninvasive, cross sectional study comprising 34 open angle glaucoma with diabetes mellitus type 2 patient participants. These patients were selected among diabetics patients with one of criteria the random serum glucose level >200 mg/dl, fasting glucose level >110 mg/dl and an HBA1C measurement >.6% in the last 6 months. Selection criteria included the presence of type 2 diabetes mellitus for less than 8 years without retinopathy. The control group consisted of 34 subjects of POAG as the same age range and sex as the open angle glaucoma with diabetic patients.. All control subjects had no history of diabetes and had undergone at least one blood exam showing normal serum glucose levelsb(<110 mg/dL) and an HbA1C measurement <6% in the last 6 months.

Ethical approval was obtained from Uniiversity Sumatera Utara ethics committee The aims and objectives of our study were explained to all participants in accordance to the

Declaration of Helsinki. A written consent was obtained from all patients by the researchers.

The participant included in open angle glaucoma with Diabetes Mellitus type 2 and POAG as a control with glaucomatous appearance of optic disc on direct ophthalmoscope, glaucomatous visual field defect on SAP confirmed on two consecutive VF test and had a history of elevated IOP.

Patients medical history was recorded, viaual acuity was measured with the best possible correction, and IOP was measured with the use of a Goldmann applanation tonometry, visual field test with Octopus 301 Perimetry. All participants underwent gonioscpy (Carl Zeiss Meditec AG, Jenna, Germany).

Inclusion criteria: We included all patients who fulfilled the following criteria : age older than 40 years old, patients diagnosed as primary open angle glaucoma (POAG), open angles, good quality scans obtained in peripapillary RNFL thickness and optic nerve head evaluation by Cirrus HD- OCT and visual field with reliable SAP.

Exclusion criteria : Criteria for the exclusion of a patient from the study were best corrected visual acuity on the Snellen Chart worse than 6/60, any ocular conditions including corneal disease and diabetic retinopathy, .

All patients had their RNFL measured by Cirrus HD- OCT (Carl Zeiss, Meditec, Dublin, CA). Cirrus HD-OCT (Carl Zeisss Meditec) improves on time-domain systems, allowing performance of up 27000 axial scans per second. Cirrus HD-OCT imaging, the Macular Cube 200 x 200 Combo protocol was used. The protocol consists of two perpendicular line scans centered at the fovea followed by a cube scan also centered at the fovea.The line scans were 6 mm in the transverse direction, had a 2 mm acial depth, and was composed of 200 x 200 axial scans. The Cirrus RNFL map represents a 6x6 mm cube of A-scan data centered over the optic nerve in which a 3.4 mm diameter circle RNFL data is extracted to create what is refered It to as the TSNIT map (temporal, superior, nasal, inferior) is displayed as a false color scale with the thickness values by quadrants and clock hours, and the RNFL peaks give a sense of the anatomic distribution of nerve fiber axons represented by the superior and inferior bundles that emanate from optic neve. .SD OCT had a sensitivity of 83% and a specificity of 88%[15,16]

Cirrus HD-OCT also automatically outlines the optic nerve head, optic cup, and disc borders similar to mental estimations by clinicians, but then also calculates more objective measurements such as optic disc area and neuroretinal rim area in addition to the classic clinician subjective average. And vertical cup to disc ratio. This allows the 3,4 mm RNFL circle to always be centered in the same spot within the cube. ONH parameters have also been found to have excellent ability to discriminate between normal eyes and eyes with even mild glaucoma. The parameters found to have the greatest diagnostic capability are vertical rim thickness, rim area, and vertical cup to disc ratio. These ONH parameters were found to be as good as RNFL thickness parameters in diagnosing glaucoma[17].

Standart automated perimetry

SAP was performed with Normal strategy on OCTOPUS 301 (Haag-Streit, InterzeagInternational AG, Schlieren, Switzerland). A reliable VF defect was defined as one with less than 33% fixation loss and less than 20% positive and negative catch trial. Glaucomatous VF defect was defined as MD >2.0 dB (equivalent to being triggered at the 5% level on the Humprey Field Analyzer) or both in at least two reliable examinations.[18]

Statistical Analysis

The collected data write in the research publication and keep in the computer. The collected data keeped in computer analysed by using the statical software. To compare quantitative variables between the two groups, one way Anova test was used. Stastical analyses were performed with SPSS 19,0 and the level significance was = 0,05 in all stastical test.

III. Results

The demographic parameters from 34 patients open angle glaucoma with diabetes mellitus and 34 patients control are presented in Table 1.

Characteristic	Open Angle Glaucoma with DM type 2 x ± SD	Primary open Angle Glaucoma x ±SD	P value
Sex			
- Men	15(52,90)	11(32,40)	
- Women	16(47,10)	23 (67,60)	
Age	47,00±8,16	50,97±9,58	0,369
IOP	19,25±8,92	18,74±9,13	0,861
BCVA	0,05 0,010	0,07±0,10	0,410
MD (dB)	4,05±1,07	3,65±0,87	0,875

Based the clinical characteristic there was no significant differences between the two groups (p>0,05).

Table 2. RNFL Thickness Measurement

RNFL parameter	Open Angle Glaucoma with DM type 2 x ± SD	Primary open Angle Glaucoma x ±SD	P value
Average			
- Mean SD	60,43± 16,68	72,32± 11,95	0,543
Inferior			
- Mean SD	75,67± 15,02	88,78± 27,83	0,469
Superior			
- Mean SD	48,78± 19,05	79,25± 14,39	0,019[8]
Nasal			
- Mean SD	57,52±	72,83±	0,12

	21,20	17,40	1
Temporal			
- Mean SD	47,74± 18,15	56,79± 8,65	0,98 5

From the table, all 5 RNFL parameters were significantly thinner in the open angle glaucoma with DM type 2 compared with POAG group, but only in the superior average statistically significant difference (p<0,05).

Table 3. ONH parameter

ONH parameter	Open Angle Glaucoma with DM type 2 x ± SD	Primary open Angle Glaucoma x ±SD	P valu e
CDR	0,72 ±,14 0	0,68 ± 0,15	0,61 2
CD Vertical	0,73 ± 0,16	0,69 ± 0,13	0,54 3
CD Horizontal	0,70 ± 0,21	0,65 ± 0,19	0,57 1

From the table, all 3 optic nerve head parameters had enlargement but statistically no significant difference (p>0,05).

IV. Discussion

Glaucoma is the second leading caused blindness after cataract in the world. Glaucoma referes to a group of diseases with optic neuropathy and decreased of visual field and higher intraocular pressure and diabetes mellitus as a risk factor[5,6,7] . Diabetic is a complex disease resuting from the inability of the body to produce insulin, a hormone that takes sugar out of the blood and into cells where it can be used for energy[1]. Diabetes mellitus may also alter the function of nonvascular cells .Exprimental studies in diabetic rats showed evidence of retinal ganglion cell loss or damage. In humans, both histological and immunohistochemical studies provided evidence of loss of retinal ganglion cells[19,20].

Qualitative photographic evaluation of RNFL in diabetic patients showed evidence of thinning. The defect was associated with advanced age and higher levels of retinopathy. Therefore the objective determination of RNFL thickness is essential. Determination of RNFL defects using OCT confirmed that the thinning is associated with the presence of diabetes mellitus[21,22]. In our study, we observed thinning of RNFL and ONH by using Cirrus HD-OCT.

Furthermore, we demonstrated that there was a statistically significant reduction in superior average in open angle glaucoma with DM type 2. Diabetes mellitus is characterized by obstruction and disruption of the basic membrane of small blood vessels. It has been hypothesized that superficial capillary vessels responsible for the perfusion of the nerve fibers and optic nerve head become ischemic. This may explain why there are early disruptions in vision, suh as reduction in contast sensitivity, impaired evoked visual dynamics and deterioration of visual fields in diabetic patients before vascular lesions are detected[23,24,25].

In previous studies from Sugimoto, thinning of RNFL was found more prominent in the superior area, and it suitable with our study that found the thinning RNFL in superior area[26].

From the optic nerve head assessment, there was not statistically significant difference in Cup/Disc Ratio Vertical, Horizontal, and Cup Disc Ratio between the two groups. Alexander Fredrich found the optic nerve morphology with stereophotography there was no statistically significant difference in open angle glaucoma with DM compared to without DM[27].

In conclusion, we found there was significant thinner of superior average RNFL in open angle glaucoma with DM type 2. Therefore, RNFL thickness in diabetic patients may prove a valuable tool in the assessment and routine monitoring and its associated visual deficits. Nonetheless, it is still premature to advocate the routine measurement of RNFL thickness as a means of detecting early changes in diabetics. Well design, good quality prospective longitudinal clinical trials on larger populations are therefore needed.

Disclosure

Patients have been approved prior to the study conducted. costs borne by researchers

References

[1] Dowers AC, Diabetes Mellitus. In : Fauci AS, Brainwald E, Hauser SL. Harrison"s Principles of Internal Medicine. 17th edition. SanFransisco: Mc Grow-Hill Company. 2008; p: 2275-2302.

[2] Jack LL. In; Pathogenesis of Type 2 Diabetes Mellitus, University of Vermont College of Medicine, Berlington, Journal of National Centre for Biotechnology Information. Volume 36, Issue 3, 2004; Page 197-209.

[3] Harrison LC, Winthworth JM, Elkassaby S, Farlanos S, Greenbaum CJ. Reappraising the Stereotypes of Diabetetes In Greenbaum CJ, Harrison LL (ed), Diabetes; Translating Research Into Practice New York: Informa Healthcare. 2008; p 193-269.

[4] Ministry of Health Republic of Indonesia. Centre of Data and Information. Indonesia Health Profile 2008. Jakarta.,2010

[5] Lisegang TJ, Gregory LS, Louis B. Glaucoma, In: American Academy of Ophthalmology Section 10, San Fransisco, 2009

[6] Kansky JJ. Clinical Ophthalmology. A Systemic Approach. fifth edition. Oxford. 2003; p 193-269

[7] Dielemans I et al. Primary Open Angle Glaucoma, Intraocular Pressure and Diabetes Mellitus in The General Elderly Population The Rotterdam Study. Journal of National Centre for Biotechnology Information. 1996; 103(8):1271-5

[8] Distelhorst, JS Hughes GM. Open Angle Glaucoma, Am Farm Physician. 2003; 1937-1944

[9] Chopra V et al. Type 2 Diabetes Mellitus and The Risk of Open Angle Glaucoma. Los Angeles Latino Eye Study. Ophthalmology Journal Impact Factor and Information. 2007; Vol 115, No2, p 227-233

[10] Fowler JM. Microvascular and Macrovascular Complication of Diabetes Mellitus. Journal of American Diabetse Association.2008

[11] Kern TS, Barber AS. Retinal Ganglion Cells in Diabets Mellitus. J.Physiol.2008; p:4401-8

[12] De Voogd S, Ikram MK, Wolfs RC, Jansonius NM, Witteman JC, et al. Is Diabetes Mellitus a Risk Factor for Open Angle Glaucoma? The Rotterdam Study. Opththalmology. 2006;113: 1827-1831 (Pubmed)

[13] Morgan JE, Waldock A, Jefrey G, Lowey A. Retinal Nerve Fiber Layer Polarimetry, Histological and Clinical Comparison. Br. J. Ophthalmolgy. 1998;82 (6), 684-690 (Pubmed)

[14] Lopes de Faria JM, Russ H, Costa VP. Retinal Nerve Layer loss in Patients With Tye 1 Diabetes Mellirus Without Retinopathy. Br J Ophthalmology. 2002;86 (7), 725-728 (Pubmed).

[15] Leung CK, Yu M, Weinreb RN. Retinal Nerve Fiber Layer Imaging with Spectral- Domain Optical Coherence Tomography, Patterns of Retinal Nerve Fiber Layer Progression, Ophthalmology. 2012;119: 1858-1866

[16] Leite MT, Rao HL, Weinreb RN, Agreement among Spectral-Domain Optical Coherence Tomography Instruments For Assessing Retnal Nerve Fiber Layer Thickness. Am J Opthalmol 2011, 151: 85-92

[17] Mwanza JC, Chang RT, Budenz DL, Reproducibility of Peripapillary Retinal Nerve Fiber Layer Thickness and Optic Nerve Head Parameters Measured with Cirrus HD-OCT in Glaucomatous Eye. Invest Ophthalmol Vis Sci, 2010; 51: 5724-5730

[18] Interzeag AG, Automated Perimetry, In : Interzeag AG, Octopus Visual Field Digest. Switzerland.1998; 8-12

[19] Abu-El-Asrar AM, Dralands L, Missoten L, Al-Jadaan IA, Geboes K. Expression of Apoptosis Markers in The Retinasof Human Subjects With Diabetes. Invest Ophthalmol Vis Sci. 2004:45(8):2760-2766 (Pub Med)

[20] Barber AJ, Lieth E, Khin SA, Antonetti DA, Buchanan AG, Gardner TW. Neural Apoptosis in The Retina During Experimental and Human Diabetes. Early Onset and Effect of Insulin. J Clin Invest. 1998: 102(4):783-791

[21] Chihara E, Matsuoka T, Ogura Y, Matsumura M. Retinal Nerve Fiber Layer Defect As An Early Manifestation of Diabetic Retinopathy, Ophthalmology. 1993; 100 (8):114-1151 (PubMed)

[22] Shahidi AM, Sampson GP, Pritchard N. Retinal Nerve Fiber Layer Thinning Associated With Diabetic Peripheral Neuropathy. Diabet Med. 2012;29(7):106-111

[23] Varkonyl TT, Peto T, Degi R. Impairment of Visual Evoked Potentials : An Early Central Manifestation of Diabetic Neuropathy? Diabetes Care. 2002;25(9):1661-1662 (PubMed)

[24] Greenstein VC, Shapiro A, Zaidi Q, Hood DC. Psychophysical Evidence For Post-Receptoral Sensitivity Loss in Diabetes. Invest Ophthalmol Vis Sci. 1992;33(10):2781-2790

[25] Sokol S, Moskowitz A, Skarf B, Evans R, Molitch M, Senior B. Contrast sensitivity in Diabetics With And Without Background Retinopathy. Arch Ophthalmol. 1985; 103(1):51-54 (PubMed)

[26] Sugimoto M, Sasoh M, Ido M, Narushima C, Uji Y. Retinal Nerve Fiber Layer Decrease During Glycemic Control in Type 2 Diabetes, Journal of Ophthalmology. 2010

[27] Alexander F. No effect of diabetes mellitus on the morphology of the optic nerve papilla in primary open angle glaucoma. Journal of National Center for Biotechnoloy Information 1998 ;212(1):37-9

AUTHORS

First Author – Masitha Dewi Sari, Department of Ophthalmology, University Of North Sumatra
Second Author – Soraya Fasya, Department of Ophthalmology, University Of North Sumatra
Third Author – Aslim D Sihotang, Department of Ophthalmology, University Of North Sumatra