COMPARISON OF OPTIC NERVE HEAD PARAMETERS IN PATIENTS OF PRIMARY OPEN ANGLE GLAUCOMA WITH AND WITHOUT DIABETES MELLITUS

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ABSTRACT

BACKGROUND

Slowly progressive auto-degenerative neuropathy and changes of the optic nerve are well known in Open angle glaucoma. Glycaemic conditions in the body importantly may effect these damages, mutually or independent of the associated ocular pathology. An objective parameter if established for determining the correlation of the both would assist to set up proper ways of diagnosis and management of patients with Diabetics with POAG.

The aim of this study is to evaluate the optic nerve head (ONH) parameters of primary open-angle glaucoma (POAG) patients with and without diabetes and to investigate the effect of the metabolic control of diabetes on ONH topography.

MATERIALS AND METHODS

A study group of 61 eyes of 61 POAG patients with type 2 diabetes mellitus and a control group of 61 eyes of 61 POAG patients without diabetes were recruited for the study. Complete ophthalmic examinations of all patients were performed and the quantitative optic disc parameters were evaluated with HbA_{1c} measurements of diabetic patients.

RESULTS

Mean RNFL thickness of the study group was statistically lower than the control group ($P<0.001$). The difference in other parameters of the OCT between the groups were insignificant. In the study group, the duration of the diabetes and HbA_{1c} were not significantly correlated to any of the OCT parameters of ONH.

CONCLUSION

The duration of diabetes and HbA_{1c} levels in diabetic population do not seem to show any significant correlation with the optic nerve head parameters and retinal nerve fibre thickness as measured with optical coherence tomography. However, larger and controlled studies are warranted to confirm these findings.

KEYWORDS

Glaucoma, Optical Coherence Tomography, Diabetes.

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BACKGROUND

The solitary term "glaucoma" describes a heterogeneous group of progressive optic neuropathies that have in common, a slow progressive degeneration of retinal ganglion cells and their axons, resulting in a characteristic structural damage to the optic disc and a concomitant pattern of visual field loss if untreated.[1]

Primary open angle glaucoma (POAG) is the most common type of glaucoma.[2] Old age,[3] a positive family history of POAG,[4] myopia,[5] central corneal thickness,[6] and ocular hypertension.[7,8] are relatively consistent risk factors for POAG.

Diabetes has been proposed as a risk factor for elevated IOP and POAG. Diabetes mellitus has been suggested to cause microvascular damage and vascular dysregulation of the retina and the optic disc, increasing the susceptibility of the optic nerve head to damage in glaucoma.[9-11] Diabetes may also result in elevated IOP and increased risk of POAG by disrupting the trabecular meshwork function.[12] Few population based studies reported a statistically significant association between diabetes and POAG.[13-16] but many others have not found a significant relationship.[17-23] A meta-analysis conducted recently by Zhao D. et al has shown a positive association between Diabetes Mellitus and glaucoma.[24]

Currently, HbA_{1c} is a widely used glycaemic marker and is considered by the American Diabetes Association, along

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with self-monitoring of blood glucose (SMBG), as the primary technique to assess glycaemic control.[25] It provides information about the degree of glucose control during the previous 8–12 weeks in the non-pregnant population.[26]

The optical coherence tomography (OCT) has been used to assess optic disk topography in clinical practice. This instrument provides in-vivo cross-sectional scans of retinal structures by the use of low-coherence interferometry. The OCT has further been shown to provide reproducible assessment of optic disk topography and retinal nerve fibre layer. Advantages of the OCT include the automated determination of the disk margin and the automated analysis of topographic parameters and retinal nerve fibre layer thickness.[27]

There are limited published data which investigate ONH parameters in diabetic POAG patients. Recent studies have documented a protective effect of Diabetes Mellitus in patients with Primary Open Angle Glaucoma.[28] Some other studies document no significant differences on ONH parameters in POAG patients with and without Diabetes Mellitus.[29] Hence, the effects of DM on ONH parameters in patients with Primary Open Angle Glaucoma still remain controversial. In our study, we aimed to compare the optic nerve head parameters using OCT in diabetic and non-diabetic patients of POAG. Also, we tried to assess the effect of disease duration and metabolic control (using HbA_{1c} measurements) on these parameters in the disease group.

MATERIALS AND METHODS

Subjects were selected among patients attending the glaucoma clinic of Venu Eye Institute and Research Centre from January 2015 to June 2016. Ethical approval was taken from the ethical committee of Venu Eye Institute and Research Centre. A valid and informed consent was taken from the patients willing to participate in the study after giving them a detailed explanation of the evaluation procedure. Patients older than 35 years with best corrected visual acuity of 20/40 or better, diagnosed with POAG with or without Diabetes Mellitus and a spherical refraction within ± 5.0 D and cylinder correction within ± 3.0 D were included in the study.

Presence of proliferative diabetic retinopathy, corneal pathology, severe media opacities (such as corneal opacity, mature cataract, vitreous opacity), optic nerve or retina pathologies other than glaucomatous optic neuropathy, inflammatory eye disease or systemic collagen disease led to exclusion of subjects from the study. All cases of angle closure glaucoma or secondary glaucoma or a history of previous intraocular surgery (including Trabeculectomy) were also excluded.

All patients had a complete ophthalmic examination, including refraction, visual acuity, slit-lamp examination, and fundus examination. IOP was measured by Goldmann Applanation Tonometer, after using Proparacaine eye drops (0.5%) and staining the eye with Fluorescein strip (fluorescein sodium I.P. 1 mg), and keeping the base reading of tonometer at 10 mmHg. Gonioscopy was performed using a Posner or Sussman 4-mirror lens. Visual field tests were performed using 24-2 SITA standard test strategy on the Humphrey field analyser. A reliable VF defect was defined as one with less than 33% fixation loss and less than 20% false positives and false negatives.

POAG diagnosis was made in the presence of increased intraocular pressure, visual field defects, and appearance of a glaucomatous optic disc with typical loss of the neuroretinal rim by slit-lamp biomicroscopy (cup-to-disc ratio > 0.7; inter-eye cup asymmetry > 0.2; or neuroretinal rim notching, focal thinning, disc haemorrhaging, or vertical elongation of the optic cup). Only patients with open anterior chamber angles on gonioscopy were enrolled.

A history of Type 2 diabetes mellitus or antidiabetic medications along with duration, was taken in all patients. HbA_{1c} measurements of diabetic patients was made.

Ultrasonic pachymetry was used for central corneal thickness measurements. Optic nerve heads were analysed with the Cirrus HD OCT.

Statistical analysis of the readings was done. Results were reported as mean ± SD with 95% confidence intervals and P=0.05 was considered as statistically significant.

RESULTS

Mean age of the subjects was 56.13 ± 8.18 years in the study group and 60.57 ± 10.75 in the control group. Male/female ratio was 32/29 in the study group and 31/30 in the control group. In the diabetic group, the mean disease duration was 7.80 ± 3.22 years and the mean levels of HbA_{1c} was 8.01 ± 1.19.

The differences in intraocular pressure, central corneal thickness, visual field MD and PSD differences between the groups were statistically insignificant (Table 1).

	Study	Control	p-value
	Mean ± SD	Mean ± SD	
IOP (mmHg)	19.66 ± 4.22	17.18 ± 21.47	0.189
CCT (microns)	518.28 ± 14.91	511.57 ± 62.99	0.210
MD	-3.24 ± 0.85	-3.55 ± 1.35	0.067
PSD	4.20 ± 0.88	4.14 ± 1.62	0.398

Table 1. Mean of Parameters in the Study and Control Groups with their Statistical Significance

Among the ONH topographic parameters on OCT, average RNFL thickness was significantly lower in POAG patients with Diabetes. For the other parameters including rim area, disc area, average cup disc ratio, vertical cup disc ratio and cup volume, the differences were statistically insignificant (Table 2).

OCT Parameter	Study	Control	p-value
	Mean ± SD	Mean ± SD	
Average RNFL thickness (microns)	85.54 ± 8.01	93.89 ± 7.53	< 0.001
Rim area (sq.mm)	1.24 ± 0.32	1.33 ± 0.37	0.074
Disc area (sq.mm)	2.13 ± 0.48	2.16 ± 0.52	0.359
Average CDR	0.69 ± 0.07	0.69 ± 0.11	0.366
Vertical CDR	0.65 ± 0.07	0.65 ± 0.11	0.410
Cup volume (cubic mm)	0.42 ± 0.19	0.45 ± 0.21	0.163

Table 2. Mean of OCT Parameters in the Study and Control Groups with their Statistical Significance

The correlation analyses in diabetic group showed that the duration of diabetes and HbA_{1c} levels were not significantly correlated to average RNFL thickness, rim area, disc area, average cup disc ratio, vertical cup disc ratio and cup volume (Table 3).

	Duration of DM (Years)		HbA_{1C}	
	Correlation Coefficient	p-value	Correlation Coefficient	p-value
Avg. RNFL thickness (microns)	0.108	0.407	-0.001	0.994
Rim area (sq.mm)	0.102	0.434	0.045	0.731
Disc area (sq.mm)	0.102	0.434	-0.106	0.416
Average CDR	-0.108	0.407	0.031	0.813
Vertical CDR	-0.094	0.471	0.050	0.702
Cup volume (cubic mm)	0.056	0.668	-0.052	0.691

Table 3. Correlation and Statistical Significance of Parameters with Duration of Diabetes and HbA_{1c} Levels

DISCUSSION

There are limited published data which investigate the ONH parameters in diabetic POAG patients. Few studies in the past show inconclusive results. Some show no effect of diabetes on optic nerve head[29] whereas others show a protective effect of diabetes on the optic nerve head.[28]

In this study, we attempted to make a comparison of Optic nerve head parameters using Optical Coherence Tomography in patients of Primary Open Angle Glaucoma with and without Diabetes Mellitus.

Sari MD et al[30] demonstrated that there was a statistically significant reduction in superior RNFL thickness in open angle glaucoma with DM Type 2. Qualitative photographic evaluation of RNFL in diabetic patients showed evidence of thinning. The defect was associated with advanced age and higher levels of retinopathy. Determination of RNFL defects using OCT confirmed that the thinning was associated with the presence of diabetes mellitus.[31]

Budde WM and Jonas JB.[29] found similar results. The two subgroups did not vary significantly ($p > 0.10$) in mean size of the optic disc, neuroretinal rim, zones alpha and beta of the parapapillary chorioretinal atrophy, and frequencies of disc haemorrhages. Patients with or without diabetes mellitus did not differ significantly in the morphology of the optic disc. They concluded that diabetes mellitus does not markedly influence planimetry assessed optic disc damage in patients with primary open angle glaucoma, if eyes with proliferative diabetic retinopathy were excluded.

In our study, we got a statistically significant difference for average RNFL thickness in diabetic patients with POAG. All other parameters like rim area, disc area, average cup-to-disc ratio, vertical cup-to-disc ratio and cup volume showed no statistically significant relationship between diabetic and non-diabetic controls. Also, none of the parameters showed a statistically significant relationship to the duration of diabetes or to the HbA_{1c} levels implying that neither of the two factors affected Optic nerve head topography.

In the study conducted by Akkaya S et al,[28] greater measurements of rim area and rim volume in diabetic POAG patients increased the likelihood that the number of optic nerve fibres in diabetic POAG patients was greater than that in non-diabetic POAG patients. They argued that optic nerve swelling may have caused increased rim area and rim volume measurements. In diabetic POAG patients, greater measurements of rim area and rim volume together with the absence of any increase in the optic cup depth led them to consider that diabetes may cause protective effect on optic nerve and retinal nerve fibres in POAG.

In the study conducted by Jeong YS et al,[32] the average RNFL thickness and other RNFL sectoral parameters (temporal, superior, nasal, and inferior thickness) did not differ significantly among groups. For the ONH parameters, including rim area, disc area, average CDR, vertical CDR, and cup volume, no differences were found between eyes with and without diabetes. In diabetic eyes, temporal RNFL thickness was positively correlated with the HbA_{1c} level. We, in our study observed that there was no correlation between RNFL thickness and HbA_{1c} levels.

There were some limitations to this study, including the small number of samples in each group. Since this study was cross-sectional in design, the causal relationship between DM and changes in the retina is indefinite. The RNFL changes in diabetic patients might have been confused with early glaucomatous changes. Most of the glaucoma patients included in this study had early stage disease, and thus the diagnostic ability of our analysis may have been generally underestimated. Finally, subjects with enlarged cup-to-disc ratio received more eye examinations than those without enlarged CDR, and consequently were more likely to have their open-angle glaucoma detected, which might have led

to overestimating the diagnostic ability of ONH in both nondiabetic and diabetic subjects.

CONCLUSION

In this study, statistically significant difference existed between average retinal nerve fibre layer thickness as measured with optical coherence tomography in POAG patients with diabetes mellitus when compared with those without diabetes. Hence, average RNFL thickness in the diabetics with POAG appears to be decreased.

The duration of diabetes and HbA_{1c} levels in diabetic population do not seem to show any significant correlation with the optic nerve head parameters and retinal nerve fibre thickness as measured with optical coherence tomography. Our finding awaits to be verified by longitudinal and larger studies.

REFERENCES

[1] Weinreb RN, Khaw PT. Primary open-angle glaucoma. Lancet 2004;363(9422):1711-1720.

[2] Peters D, Bengtsson B, Heijl A. Lifetime risk of blindness in open-angle glaucoma. Am J Ophthalmol 2013;156(4):724-730.

[3] Leske MC, Connell AM, Schachat AP, et al. The Barbados eye study. Prevalence of open angle glaucoma. Arch Ophthalmol 1994;112(6):821–829.

[4] Sommer A, Tielsch JM. Risk factors for open-angle glaucoma: the Barbados eye study. Arch Ophthalmol 1996;114(2):235.

[5] Topouzis F, Wilson MR, Harris A, et al. Risk factors for primary open-angle glaucoma and pseudoexfoliative glaucoma in the Thessaloniki eye study. Am J Ophthalmol 2011;152(2):219-228.e1.

[6] Francis BA, Varma R, Chopra V, et al. Intraocular pressure, central corneal thickness, and prevalence of open-angle glaucoma: the Los Angeles Latino eye study. Am J Ophthalmol 2008;146(5):741-746.

[7] Heijl A, Leske MC, Bengtsson B, et al. Reduction of intraocular pressure and glaucoma progression. Arch Ophthalmol 2002;120(10):1268-1279.

[8] Kass MA, Heuer DK, Higginbotham EJ, et al. The ocular hypertension treatment study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol 2002;120(6):701-713.

[9] Hayreh SS. Pathogenesis of optic nerve damage and visual field deficits in glaucoma. Docum Ophthal Proc Series 1980;22:89–110.

[10] Nakamura M, Kanamori A, Negi A. Diabetes mellitus as a risk factor for glaucomatous optic neuropathy. Ophthalmologica 2005;219:1–10.

[11] Kanamori A, Nakamura M, Mukuno H, et al. Diabetes has an additive effect on neural apoptosis in rat retina with chronically elevated intraocular pressure. Current Eye Research 2004;28(1):47-54.

[12] Sato T, Roy S. Effect of high glucose on fibronectin expression and cell proliferation in trabecular meshwork cells. Invest Ophthalmol Vis Sci 2002;43(1):170–175.

[13] Chopra V, Varma R, Francis BA, et al. Type 2 diabetes mellitus and the risk of open-angle glaucoma: the Los Angeles Latino eye study. Ophthalmology 2008;115(2):227-232, e1.

[14] Klein BE, Klein R, Jensen S. Open-angle glaucoma and older-onset diabetes. Ophthalmology 1994;101(7):1173-1177.

[15] Mitchell P, Smith W, Chey T, et al. Open-angle glaucoma and diabetes: the Blue Mountains eye study, Australia. Ophthalmology 1997;104(4):712-718.

[16] Pasquale LR, Kang JH, Manson JE, et al. Prospective study of type 2 diabetes mellitus and risk of primary open-angle glaucoma in women. Ophthalmology 2006;113(7):1081-1086.

[17] de Voogd S, Ikram MK, Wolfs RC, et al. Is diabetes mellitus a risk factor for open-angle glaucoma? The Rotterdam study. Ophthalmology 2006;113(10):1827-1831.

[18] Le A, Mukesh B, McCarty C, et al. Risk factors associated with the incidence of open-angle glaucoma: the visual impairment project. Invest Ophthalmol Vis Sci 2003;44(9):3783-3789.

[19] Leske M, Connell AMS, Suh-Yuh Wu, et al. Risk factors for open-angle glaucoma the Barbados eye study. Arch Ophthalmol 1995;113(7):918-924.

[20] Quigley HA, West SK, Rodriguez J, et al. The prevalence of glaucoma in a population-based study of Hispanic subjects: Proyecto VER. Arch Ophthalmol 2001;119(12):1819-1826.

[21] Vijaya L, George R, Baskaran M, et al. Prevalence of primary open-angle glaucoma in an urban south Indian population and comparison with a rural population. The Chennai Glaucoma Study. Ophthalmology 2008;115(4):648-654.e1.

[22] Xu L, Xie XW, Wang YX, et al. Ocular and systemic factors associated with diabetes mellitus in the adult population in rural and urban China. The Beijing Eye Study. Eye(Lond) 2008;23(3):676-682.

[23] Tielsch JM, Katz J, Quigley HA, et al. Diabetes, intraocular pressure, and primary open-angle glaucoma in the Baltimore eye survey. Ophthalmology 1995;102(1):48-53.

[24] Zhao D, Cho J, Kim MH, et al. Diabetes, fasting glucose, and the risk of glaucoma: a meta-analysis. Ophthalmology 2015;122(1):72-78.

[25] Executive summary: standards of medical care in diabetes--2012. Diabetes Care 2012;35(Suppl 1):S4-S10.

[26] Goldstein DE. Is glycosylated hemoglobin clinically useful? N Engl J Med 1984;310(6):384-385.

[27] Hoffmann EM, Zangwill LM, Crowston JG, et al. Optic disk size and glaucoma. Surv Ophthalmol 2007;52(1):32-49.

[28] Akkaya S, Can E, Öztürk F. Comparison of optic nerve head topographic parameters in patients with primary

open-angle glaucoma with and without diabetes mellitus. Journal of Glaucoma 2016;25(1):49-53.
[29] Budde WM, Jonas JB. No effect of diabetes mellitus on the morphology of the optic nerve papilla in primary open angle glaucoma. Klin Monbl Augenheilkd 1998;212(1):37–39.
[30] Sari MD, Fasya S, Sihotang AD. Retinal nerve fiber layer thickness and optic nerve head parameters in open angle glaucoma with diabetes mellitus type 2. International Journal of Scientific and Research Publications 2016;6(3):31-34.
[31] Chihara E, Matsuoka T, Ogura Y, et al. Retinal nerve fiber layer defect as an early manifestation of diabetic retinopathy. Ophthalmology 1993;100(8):1147-1151.
[32] Jeong SY, Park SJ, Chin HS, et al. Spectral-domain optical coherence tomography features in open-angle glaucoma with diabetes mellitus and inadequate glycemic control. Investigative Ophthalmology & Visual Science 2016;57(7):3024-3031.