

## Comparison of Retinal Nerve Fiber Layer Thickness in Patients of Type 2 Diabetes Mellitus and Patients of Type 2 Diabetes Mellitus Suffering From Primary Open Angle Glaucoma

Dhull V K<sup>1\*</sup>, Bishnoi Marisha<sup>2</sup>, Sachdeva Sumit<sup>1</sup>, Aggrawal Sameer<sup>3</sup>

<sup>1</sup>Professor, RIO, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, SH 16A, Haryana 124001, India

<sup>2</sup>Resident, RIO, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, SH 16A, Haryana 124001, India

<sup>3</sup>Professor, Department of Medicine, Pandit Bhagwat Dayal Sharma Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, SH 16A, Haryana 124001, India

\*Corresponding author: Dhull V K

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### Abstract

Retinal nerve fiber layer thickness is affected in several ocular and systemic conditions, most commonly glaucoma and diabetic retinopathy. The present cross sectional study was conducted to compare the retinal nerve fiber layer thickness in patients of type 2 diabetes mellitus, and patients of primary angle glaucoma suffering from type 2 diabetes mellitus. A total of 120 consecutive eyes of 60 patients were assigned to 2 groups of 30 patients each of type 2 diabetes mellitus and patients of primary open angle glaucoma suffering from type 2 diabetes mellitus. Retinal nerve fiber layer thickness was measured with spectral-domain optical coherence tomography. Readings from all the areas of retina (superior nasal, inferior nasal, inferior temporal, superior temporal, nasal upper, nasal lower, temporal lower, temporal upper) were measured in both eyes. The presence of type 2 diabetes mellitus in patients of primary open angle glaucoma significantly affected the thickness of retinal nerve fiber layer specially in superonasal and inferotemporal quadrants as compared to patients of primary open angle glaucoma or diabetes mellitus individually. RNFLT is negatively correlated with the duration of glaucoma, duration of diabetes and HbA1c levels. Hence care should be taken in interpreting optical coherence tomography readings in patients of primary open angle glaucoma having diabetes mellitus, and such patients should not be over treated. The changes in retinal nerve fiber layer thickness can be used to monitor the progression or regression of diseases affecting nerve fiber layer and efficacy of treatment modalities in individual cases.

**Keywords:** Applanation tonometry, electroretinography, HbA1c levels, intraocular pressure, optical coherence tomography, Optic nerve head changes, Retinal ganglion cells, Scanning laser polarimetry.

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### INTRODUCTION

Normal vision depends on the proper functioning of the retinal neurons in order to produce a good quality of image. Retinal nerve fiber layer (RNFL) is an important structure in the retina, which is affected, in the early stages of various ocular and systemic morbidities. The RNFL comprises of retinal ganglion cell (RGC) axons, neuroglia and astrocyte. The RNFL thickness (RNFLT) is affected in several ocular and systemic conditions, most commonly glaucoma and diabetic mellitus. Evaluation of RNFLT as a mean of assessing optic nerve health has been a well-established clinical and investigational tool [1].

Glaucoma is an optic neuropathy, which is characterized by ganglion cell death, which presents clinically as characteristic optic nerve head (ONH) and/or RNFLT changes with correlating visual field

defects. Primary open angle glaucoma (POAG) is the most common form of glaucoma. It is usually bilateral, although it may be asymmetric in the two eyes. Soliman *et al.* found that Retinal nerve fiber loss precedes measurable ONH changes and visual field defects and is observed in 60% patients, approximately six years before any detectable visual field defects in glaucoma [2].

Examination of the ONH and its surrounding RNFL is considered essential in the diagnosis as well as monitoring of glaucoma. Damage to the optic disc is associated with an abnormal appearance of RNFL. Retinal nerve fiber layer defects have two patterns-localized wedge defects and diffuse loss recognized in glaucoma patients. Localized loss is more easily and consistently recognized, but is less common.

There are various techniques, as suggested by Greaney *et al.* such as confocal scanning laser polarimetry (GDx with variable corneal compensation) and Optical coherence tomography (OCT), which help in quantitative, reproducible and objective measurement of ONH and RNFLT [3].

Diabetes mellitus is a metabolic disorder. Type 2 DM is more common than type 1. Most important microvascular complication of DM includes diabetic retinopathy. As observed by Lin *et al.*, Abscower *et al.* and Sahin *et al.* in addition to vascular changes, the earlier stages of diabetic retinopathy (DR) causes neurodegenerative changes such as loss of RGC, glial cell reactivity and thinning of RNFL [4-6]. In recent clinical and experimental studies it has been observed that these neurodegenerative changes cause abnormalities in the electroretinogram (ERG), contrast sensitivity, dark adaptation and microperimetry [7]. Demir *et al.* and Takis *et al.* on the basis of histological and immunohistochemical studies have reported that DR affects retinal ganglion cells, horizontal cells, amacrine cells and photoreceptor in the neural retina and results in significant decrease in RNFLT [8, 9]. Baumann *et al.* used Spectral-domain OCT (SD-OCT) to show that RNFL thinning in DR is due to RGC loss [10].

The OCT is a non-invasive tool for objective, real-time, quantitative, high resolution (approximately up to 10 $\mu$ ) measurement and cross sectional imaging of retina with high reproducibility, reliability. Huang *et al.* noted that from OCT images RNFLT could be calculated by using low-coherence interferometry [11]. The OCT uses a computer fed algorithm to calculate RNFLT. Presence of conditions like hazy media, high astigmatism, dense cataract, asteroid hyalosis and poor fixation can compromise the quality of tomogram.

Attempts have been made by Demir *et al.* to find the correlations between thinning of RNFLT and age, sex, duration of POAG, status of intraocular pressure control, duration of diabetes, disease stage and glycemic control [8].

Till now, researchers have been evaluating RNFLT in patients with glaucoma (both POAG and normal tension glaucoma) and patients of T2DM separately. To the best of our knowledge literature search showed that no study has been conducted to correlate changes in RNFLT in patients of POAG and DM. Hence this study was carried out to evaluate the effect of POAG on RNFLT in patients of DM and compare it with RNFLT in patients having only type 2 DM.

## MATERIALS AND METHODS

The present cross sectional study was carried out on 60 patients in a tertiary eye care institute in northern India. A total of 60 patients were divided in

two groups of thirty patients each having T2 DM, and patients of POAG with T2 DM respectively. The patients of both sexes, and age group of 30 to 70 years, attending glaucoma and diabetes clinic were enrolled in this study. All patients had best corrected visual acuity (BCVA) of 20/40 (6/12) or better, and open anterior chamber angles. The patients were divided into three groups and the following inclusion and exclusion criteria were applied respectively:

In group I, 30 patients of type 2 Diabetes mellitus (T 2 DM) having the following characteristics for more than 5 years were included: blood glucose levels  $\geq$  126 mg/dl (fasting) or  $\geq$  200 mg/dl (post prandial) according to ADA. The patients having intraocular pressure  $>$  21 mmHg (without any treatment) or  $<$ 21 mmHg (on anti-glaucoma treatment), glaucomatous field changes and glaucomatous disc changes were excluded from this group

In group II, patients of POAG having T 2 DM having any two of the following characteristic for 1-3 years were included: i) IOP  $>$  21mmHg (without glaucoma treatment) or  $<$  21mmHg (on anti-glaucoma treatment), ii) glaucomatous field defects or iii) glaucomatous disc changes. And all patients having the following characteristics for more than 5 years were also included: Blood glucose levels  $\geq$  126 mg/dl (fasting) or  $\geq$  200 mg/dl (post prandial) according to ADA.

The following exclusion criteria were applied to all the three groups: anterior chamber angle abnormalities on gonioscopy, any other intraocular disease except those mentioned in the inclusion criteria, secondary causes of IOP increase (pseudoexfoliation, corticosteroid use, iridocyclitis, trauma), any kind of laser fundus photocoagulation in the past, retinal disease, such as branch or central vein occlusion, central retinal artery occlusion, age related macular degeneration, macular hole or epiretinal membrane, high myopia, previous refractory surgeries, history of major intraocular surgery, corneal opacity or dense cataract.

An informed consent was taken in all cases. A detailed history regarding demographic features, predisposing factors, associated ocular conditions, systemic diseases like hypertension, cardiovascular diseases (e.g., stroke, coronary artery disease, peripheral artery disease), any kind of medications (systemic or topical) was taken. Best corrected visual acuity (BCVA), slit lamp examination, applanation tonometry, gonioscopy, visual field analysis using Humphry visual field analyser and detailed fundus examination using direct and indirect ophthalmoscopy and slit lamp biomicroscopy using +90 D lens was done.

Optical coherence tomography was done on spectral-domain OCT (SD-OCT) machine (RTVue, model-RT100 of OPTOVUE Inc. FREEMONT, CALIFORNIA, USA), software version 5.0. After dilating the pupil, multiple scans were taken. The RNFLT was calculated using glaucoma protocol. Two circular scans, each 3.4 mm in diameter centered on the optic disc, were obtained in each patient. The best quality and properly aligned scans were used for analysis. The RNFLT was calculated globally and separately for superior, inferior, temporal and nasal quadrants. We also calculated the RNFLT for all 16 sectors of RNFL.

The data was entered in Microsoft excel spreadsheet and statistical analysis was performed by using SPSS (Statistical Package for the Social Sciences) software version 21.0 (SPSS Inc., Chicago, IL). Clinical data were expressed as mean  $\pm$  standard deviation (SD) and percentage (%). The difference was considered significant when the p value was  $< 0.05$  (two sided).

## RESULTS AND DISCUSSION

In the present study age distribution in the groups was as shown in Table-1.

**Table-1: Age Distribution of cases in group I and II**

Age groups (years)	Group I (T2DM) (n=30)	Group II (POAG+T2DM) (n=30)
<30	0	0
31-40	4	0
41-50	7	4
51-60	11	10
>60	8	16
Range	31-70	42-70
Mean $\pm$ SD	54.06 $\pm$ 9.84	61.13 $\pm$ 8.27

On statistical analysis, the difference between the two groups was significant.

The sex distribution in the two groups was as shown in Table-2.

**Table-2: Sex distribution of cases in the two groups**

Sex	Group I (T2DM)	Group II (POAG+T2DM)
Male	16 (53.30%)	15 (50%)
Female	14 (46.70%)	15 (50%)

On statistical analysis sex distribution was not significant between the groups.

The mean duration of POAG in group II was as shown in Table-3.

**Table-3: Mean duration of POAG in group II**

Duration	Group II (POAG+T2DM)
Mean $\pm$ SD (years)	2.03 $\pm$ 0.85

The mean duration of DM in group I and II was as depicted in Table-4.

**Table-4: Mean duration of DM in the two groups**

Duration	Group I (T2DM)	Group II (POAG+T2DM)	p value I vs. II
Mean $\pm$ SD (years)	9.40 $\pm$ 4.47	9.93 $\pm$ 4.27	0.640 NS

vs.= versus, NS= Not significant

Duration of diabetes was not statistically different between group I and II.

The routine laboratory investigations to see the status of DM were done (Table-5).

**Table-5: Routine laboratory investigations for Type 2 DM in group I and II**

Investigations	Group I (T2DM) (mean ± SD)	Group II (POAG+ T2DM) (mean ± SD)	p value I vs. II
Fasting plasma glucose (mg/dl)	147.96 ± 34.90	166 ± 40.81	0.020 Sig.
Post prandial plasma glucose (mg/dl)	220 ± 72.31	255.03 ± 72.96	0.040 Sig.
HBA1c (%)	7.54 ± 1.65	8.22 ± 1.52	0.103 NS
S. creatinine (mg/dl)	1.65 ± 0.82	1.84 ± 0.67	0.332 NS

vs.= Versus, Sig.= Significant, NS= Not significant

Fasting and postprandial blood sugar, HBA1c and serum creatinine were found to be lower in group I as compared to group II, but on statistical analysis only blood sugar was found to be significantly lower.

Retinal nerve fiber layer thickness of right eye was as shown in Table-6.

**Table-6: Mean superior nasal RNFLT of RE in the two groups**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Superior nasal RNFLT (mean±SD) (µm)	113.1±21.53	96.16±16.33	0.001 Sig.

µm= micrometer

On analysis, the difference between groups I and II was found to be significant.

**Table-7: Mean nasal upper RNFLT of RE in the two groups**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Nasal upper RNFLT (mean±SD) (µm)	76.96±12.82	64.03±16.45	0.001 Sig.

On statistical analysis, the difference between groups I and II was significant.

**Table-8: Mean nasal lower RNFLT of RE in two groups**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Inferior nasal RNFLT (mean±SD) (µm)	124.33±21.68	110.13±29.67	0.03 Sig.

On statistical analysis, the difference between groups I and II, was significant.

**Table-9: Mean inferior temporal RNFLT of RE in the two groups**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Inferior temporal RNFLT (mean±SD) (µm)	143.9±27.04	126.5±32.89	0.02 Sig.

On statistical analysis, the difference between group I and II was significant.

**Table-10: Mean temporal lower RNFLT of RE in group I and II**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Temporal lower RNFLT (mean±SD) (µm)	77.53±14.35	70.06±17.75	0.07 NS

On statistical analysis the difference between the two groups was insignificant.

**Table-11: Mean temporal upper RNFLT of RE in two groups**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Temporal upper RNFLT (mean±SD) (µm)	84.36±18.76	76.43±21.27	0.131 NS

On statistical analysis the difference amongst the three groups was found to be comparable and thus insignificant.

**Table-12: Mean superior temporal RNFLT of RE in group I and II**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Superior temporal RNFLT (mean±SD) (μm)	131.86±20.04	115.53±21.65	0.003 Sig.

On statistical analysis, the difference between group I and II was significant.

**Table-13: Mean superior nasal RNFLT of LE in group I and II**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Superior nasal RNFLT (mean±SD) (μm)	123.23±16.82	102.63±20.97	0.001 Sig.

On statistical analysis, the difference between group I and II was significant.

**Table 14. Mean nasal upper RNFLT of left eye in group I and II**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Nasal upper RNFLT (mean±SD) (μm)	80.20±15.84	74.20±18.30	0.179 NS

On statistical analysis the difference between the two groups was insignificant.

**Table-15: Mean nasal lower RNFLT of LE in two groups**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Nasal lower RNFLT (mean±SD) (μm)	74.96±13.32	69.43±19.82	0.209 NS

On statistical analysis the difference between the two groups was insignificant.

**Table-16: Mean inferior nasal RNFLT of LE in group I and II**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Inferior nasal RNFLT (mean±SD) (μm)	134.16±22.22	121.60±32.78	0.08 NS

On statistical analysis, the difference between groups I and II was insignificant.

**Table-17: Mean inferior temporal RNFLT of LE in two groups**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Inferior temporal RNFLT (mean±SD) (μm)	132.66±20.11	117.00±26.83	0.01 Sig.

On statistical analysis, the difference between group I and II was significant.

**Table-18: Mean temporal lower RNFLT of LE in group I and II**

Parameter	Group I (T2DM)	Group II (T2DM+POAG)	p value I vs. II
Temporal lower RNFLT (mean±SD) (μm)	66.96±10.28	64.00±12.92	0.329 NS

On statistical analysis the difference between the two groups was insignificant.

**Table-19: Mean temporal upper RNFLT of LE in two groups**

Parameter	Group I (T2DM)	Group II (T2DM + POAG)	p value I vs. II
Temporal upper RNFLT (mean±SD) (µm)	78.03±15.37	73.26±16.19	0.247 NS

On statistical analysis the difference between group I and II was found to be insignificant

**Table-20: Mean superior temporal RNFLT of LE in the two groups**

Parameter	Group I (T2DM)	Group II (T2DM + POAG)	p value I vs. II
Superior temporal RNFLT (mean±SD) (µm)	132.76±19.82	117.16±24.67	0.001 Sig.

On statistical analysis, the difference between group I and II was significant.

The correlation between duration of DM and RNFLT of RE and LE of group I was analysed using Pearson’s coefficient of correlation (Table-21).

**Table-21: Correlation between duration of DM and RNFLT in RE and LE of group I**

Parameter	RE			LE		
	R value	p value	Statistical Significance	R value	p value	Statistical Significance
Superior nasal RNFLT	-0.255	>0.05	NS	-0.623	<0.01	Sig.
Nasal upper RNFLT	-0.326	>0.05	NS	-0.554	<0.01	Sig.
Nasal lower RNFLT	-0.287	>0.05	NS	-0.435	<0.05	Sig.
Inferior nasal RNFLT	-0.332	>0.05	NS	-0.224	>0.05	NS
Inferior temporal RNFLT	-0.280	>0.05	NS	-0.292	>0.05	NS
Temporal lower RNFLT	-0.253	>0.05	NS	-0.243	>0.05	NS
Temporal upper RNFLT	-0.263	>0.05	NS	-0.202	>0.05	NS
Superior temporal RNFLT	-0.202	>0.05	NS	-0.358	>0.05	NS

Sig.= Significant, NS= Not significant

When correlated duration of diabetes with RNFLT of LE in group I, superior nasal, nasal upper nasal lower RNFLT was found to be negatively correlated and statistically significant (p <0.05). But, with regard to the RE, all of the sectors of RNFLT were

found to be negatively correlated and statistically insignificant (p> 0.05)

The correlation between duration of DM and RNFLT of RE and LE of group I was analysed using Pearson’s coefficient of correlation (Table-22).

**Table-22: Correlation between duration of diabetes and RNFLT of RE and LE in group I**

Parameter	RE			LE		
	R value	p value	Statistical Significance	R value	p value	Statistical Significance
Superior nasal RNFLT	-0.511	<0.01	Sig.	-0.450	<0.01	Sig.
Nasal upper RNFLT	-0.562	<0.01	Sig.	-0.659	<0.01	Sig.
Nasal lower RNFLT	-0.549	<0.01	Sig.	-0.510	<0.01	Sig.
Inferior nasal RNFLT	-0.592	>0.01	Sig.	-0.297	>0.05	NS

Inferior temporal RNFLT	-0.639	>0.01	Sig.	-0.489	<0.01	Sig.
Temporal lower RNFLT	-0.478	>0.01	Sig.	-0.458	<0.05	Sig.
Temporal upper RNFLT	-0.566	>0.01	Sig.	-0.486	<0.01	Sig.
Superior temporal RNFLT	-0.618	>0.01	Sig.	-0.623	<0.01	Sig.

When correlated the duration of diabetes with RNFLT of RE in group I, all the sectors of RNFLT were found to be negatively correlated and statistically significant (p <0.01). Similarly, when correlated with

LE, all the sectors of RNFLT except inferior nasal were found to be negatively correlated and statistically significant (p <0.05).

**Table-23: Correlation between duration of glaucoma and RNFLT of RE and LE Of group II**

Parameter	RE			LE		
	R value	P value	Statistical Significance	R value	P value	Statistical Significance
Superior nasal RNFLT	0.370	<0.05	Sig.	-0.123	>0.05	NS
Nasal upper RNFLT	0.345	>0.05	NS	-0.271	>0.05	NS
Nasal lower RNFLT	-0.416	<0.05	Sig.	-0.179	>0.05	NS
Inferior nasal RNFLT	-0.213	>0.05	NS	-0.700	>0.05	NS
Inferior temporal RNFLT	-0.375	<0.05	Sign.	-0.178	>0.05	NS
Temporal lower RNFLT	-0.261	>0.05	NS	-0.251	>0.05	NS
Temporal upper RNFLT	-0.435	<0.05	Sig.	-0.426	<0.05	Sig.
Superior temporal RNFLT	-0.484	<0.01	Sig.	-0.423	<0.05	Sig.

When correlated, duration of glaucoma with RNFLT of right eye, nasal lower, inferior temporal, temporal upper and superior temporal were negatively correlated and statistically significant (p <0.050). When

compared with left eye, only temporal upper and superior temporal were negatively correlated and statistically significant.

**Table-24: Correlation between HbA1c and RNFL thickness of RE and LE of group I**

Parameter	RE			LE		
	R value	P value	Statistical Significance	R value	P value	Statistical Significance
Superior nasal RNFLT	-0.169	>0.05	NS	-0.365	<0.05	Sig.
Nasal upper RNFLT	-0.243	>0.05	NS	-0.287	>0.05	NS
Nasal lower RNFLT	0.070	>0.05	NS	-0.366	<0.05	Sig.
Inferior nasal RNFLT	-0.100	>0.05	NS	-0.345	>0.05	NS
Inferior temporal RNFLT	-0.470	>0.05	NS	-0.207	>0.05	NS
Temporal lower RNFLT	-0.047	<0.01	Significant	0.070	>0.05	NS
Temporal upper RNFLT	-0.430	<0.01	Significant	-0.183	>0.05	NS
Superior temporal RNFLT	-0.614	<0.01	Significant	-0.310	>0.05	NS

When correlated HbA1c with the RNFLT of the right eye in group I, temporal lower, temporal upper and superior temporal RNFLT was negatively correlated and statistically significant (p<0.01). When

similar comparison was made with left eye in group II, superior nasal and nasal lower RNFLT was negatively correlated and statistically significant (p value<0.05).

**Table-25: Correlation between HbA1c and RNFL thickness of RE and LE of group II**

Parameter	RE			LE		
	R value	P value	Statistical significance	R value	P value	Statistical significance
Superior nasal RNFLT	-0.321	>0.05	NS	-0.435	<0.05	Significant
Nasal upper RNFLT	-0.271	>0.05	NS	-0.437	<0.05	Significant
Nasal lower RNFLT	-0.242	>0.05	NS	-0.236	>0.05	NS
Inferior nasal RNFLT	-0.282	>0.05	NS	-0.095	>0.05	NS
Inferior temporal RNFLT	-0.283	>0.05	NS	-0.137	>0.05	NS
Temporal lower RNFLT	-0.268	>0.05	NS	-0.435	<0.05	Significant
Temporal upper RNFLT	-0.382	<0.05	Significant	-0.407	<0.05	Significant
Superior temporal RNFLT	-0.335	>0.05	NS	-0.269	>0.05	NS

When correlated HbA1c with RNFLT of right eye, temporal upper RNFLT was found to be negatively correlated and statistically significant ( $p < 0.05$ ). When similar comparison was made with left eye, superior nasal, nasal upper, temporal lower and temporal upper RNFLT also found to be negatively correlated and was statistically significant ( $p < 0.05$ ).

Retinal nerve fiber layer thickness was measured in all areas of right eye. Except for inferior nasal, all areas showed more thinning of RNFL in patients of POAG with DM > T2DM group. This difference was statistically significant in all areas except for temporal upper and temporal lower. In the left eye, superior nasal, nasal upper, inferior temporal and temporal lower areas showed more thinning of RNFL in patients of POAG with DM > T2DM group. Rest of the areas showed RNFL thinning in the order POAG with T2DM > T2DM

Various studies have reported significant loss of RNFL in patients of POAG as well as in patients of type 2 DM, but none have studied it in patients of POAG having Type 2 DM and compared the three groups. In the present study we evaluated the magnitude of decrease in RNFLT in patients of type 2 DM and patients of POAG with type 2 DM and compared the two groups.

In the present study mean age of the patients was 59.60 years. The age difference between the two groups was not statistically significant. Mean age in the present study was close to that reported by Takis *et al.* and Demir *et al.* [8, 9].

The sex distribution in the present study was comparable in the two groups with no statistically significant difference. It was similar to the studies

conducted by Demir *et al.*, Ramakrishanan *et al.* and Sari *et al.* [9, 12, 13].

The mean duration of POAG in this study was 2.03 years. We found a negative correlation between duration of glaucoma and RNFLT. Studies carried out by various investigators support our finding that in glaucomatous eyes RNFL thickness decreases with duration of glaucoma [14-18].

Mean duration of diabetes in-group I and II was comparable. We found a negative correlation between duration of DM and RNFLT. Two studies in the past found that RNFL thinning was seen in early stages and accelerated by the progression of diabetic retinopathy [18, 19]. Literature search showed that no study in the past has evaluated the effect duration of DM and plasma glucose levels on RNFLT.

In the present study, we observed that patients having POAG with T2 DM had statistically significant RNFL damage compared to those having T2 DM. The damage was more pronounced in the superior quadrant. A study conducted by Sari *et al.* found that the RNFL was thinner in patients of POAG with DM compared to type 2 DM patients. Particularly, the superior quadrant was affected the most as in the present study [13]. Several other studies conducted in the past comparing RNFL thinning individually in the above two groups compared to the normal support the findings of the present study [9,14, 20-22].

We also found a negative correlation between HbA1c and RNFLT. One study by Funatsu *et al.* go against our findings by reporting that there was a worsening of RNFLT after good glycemic control [23]. Nor- Sharina *et al.* conducted a cross sectional study and observed a positive correlation between HbA1c and



RNFL thickness [24]. More studies are needed to find the effect of glycemic control on RNFLT.

Limitations of the present study are a smaller sample size, single centre study and being a cross sectional study no follow-up was done. So, a multicentric study with a larger sample size and subsequent follow up of the patients to monitor the effects glaucoma and glycemic control is required to generalize the results.

## CONCLUSION

We conclude that type 2 diabetes mellitus (T2 DM) and primary open angle glaucoma (POAG) suffering from T2 DM cause retinal nerve fiber layer thinning. Further, the presence of type 2 DM in patients of POAG significantly affects the thickness of RNFL specially in superonasal and inferotemporal quadrants as compared to patients of DM. Retinal nerve fiber layer is negatively correlated with the duration of glaucoma, duration of diabetes and HbA1c levels. Hence, care should be taken in interpreting OCT findings in patients of POAG having DM, and such patients should not be over treated. The limitations of this study are small sample size, single centre research and lack of follow up of the study population. Hence, a multicentric, longitudinal study with larger sample size will be better able to corroborate our findings.

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## REFERENCES

1. Skarf, B. (2002). Retinal nerve fiber loss in diabetes mellitus without retinopathy. *British Journal Ophthalmol*, 86(7), 709.
2. Soliman, M. A., Van Den Berg, T. J., Ismaeil, A. A. A., De Jong, L. A., & De Smet, M. D. (2002). Retinal nerve fiber layer analysis: relationship between optical coherence tomography and red-free photography. *American journal of ophthalmology*, 133(2), 187-195.
3. Greaney, M. J., Hoffman, D. C., Garway-Heath, D. F., Nakla, M., Coleman, A. L., & Caprioli, J. (2002). Comparison of optic nerve imaging methods to distinguish normal eyes from those with glaucoma. *Investigative ophthalmology & visual science*, 43(1), 140-145.
4. Abcouwer, S. F., & Gardner, T. W. (2014). Diabetic retinopathy: loss of neuroretinal adaptation to the diabetic metabolic environment. *Annals of the New York Academy of Sciences*, 1311(1), 174-190.
5. Sahin, S. B., Sahin, O. Z., Ayaz, T., Karadag, Z., Turkyilmaz, K., & Aktas, E. (2014). The relationship between retinal nerve fiber layer thickness and carotid intima media thickness in patients with type 2 diabetes mellitus. *Diabetes Res Clin Pract*, 106(30), 583-589.
6. Lim, M. C., Tanimoto, S. A., Furlani, B. A., Lum, B., Pinto, L. M., Eliason, D., ... & Melo, L. A. (2009). Effect of diabetic retinopathy and panretinal photocoagulation on retinal nerve fiber layer and optic nerve appearance. *Archives of Ophthalmology*, 127(7), 857-862.
7. Van Dijk, H. W., Verbraak, F. D., Kok, P. H., Stehouwer, M., Garvin, M. K., Sonka, M., ... & Abramoff, M. D. (2012). Early neurodegeneration in the retina of type 2 diabetic patients. *Investigative ophthalmology & visual science*, 53(6), 2715-2719.
8. Demir, M., Oba, E., Sensoz, H., & Ozdal, E. (2014). Retinal nerve fiber layer and ganglion cell complex thickness in patients with type 2 diabetes mellitus. *Indian journal of ophthalmology*, 62(6), 719-720.
9. Takis, A., Alonistiotis, D., Panagiotidis, D., Ioannou, N., Papaconstantinou, D., & Theodossiadis, P. (2014). Comparison of the nerve fiber layer of type 2 diabetic patients without glaucoma with normal subjects of the same age and sex. *Clinical ophthalmology (Auckland, NZ)*, 8, 455-463.
10. Baumann, M., Gentile, R. C., Liebmann, J. M., & Ritch, R. (1998). Reproducibility of retinal thickness measurements in normal eyes using optical coherence tomography. *Ophthalmic Surgery, Lasers and Imaging Retina*, 29(4), 280-285.
11. Huang, D., Swanson, E. A., Lin, C. P., Schuman, J. S., Stinson, W. G., Chang, W., ... & Puliafito, C. A. (1991). Optical coherence tomography. *science*, 254(5035), 1178-1181.
12. Ramakrishnan, R., Mittal, S., Ambtkar, S., & Kader, M. A. (2006). Retinal nerve fiber layer thickness in normal Indian population by optical coherence tomography. *Indian Journal Ophthalmol*, 54, 11-15.
13. Sari, M. D., Fasya, S., & Sihotang, A. D. (2016). Retinal nerve fiber layer thickness and optic nerve head parameters in open angle glaucoma with diabetes mellitus type 2. *International Journal Science Research*, 6(3), 31-34.
14. Hoyt, W. F., Schlicke, B., & Eckelhoff, R. J. (1972). Fundoscopic appearance of nerve-fiber-bundle defect. *British Journal of Ophthalmology*, 56(8), 577-583.
15. Subbiah, S., Sankarnarayanan, S., Thomas, P. A., & Jesudasan, C. N. (2007). Comparative evaluation of optical coherence tomography in glaucomatous, ocular hypertensive and normal eyes. *Indian journal of ophthalmology*, 55(4), 283.
16. Leung, C. K. S., Cheung, C. Y. L., Weinreb, R. N., Qiu, K., Liu, S., Li, H., ... & Lam, D. S. C. (2010). Evaluation of retinal nerve fiber layer progression in glaucoma: a study on optical coherence tomography guided progression

- analysis. *Investigative ophthalmology & visual science*, 51(1), 217-222.
17. Corsi, C., Arrico, L., Iozzo, N., Montaldi, F., & De Gregorio, F. (2011). Retinal Nerve Fiber Layer Changes Evaluated by Optical Coherent Tomography in Glaucomatous Hyperopic Eyes. *Investigative Ophthalmology & Visual Science*, 52(14), 4464-4464.
  18. Carpineto, P., Toto, L., Aloia, R., Ciciarelli, V., Borrelli, E., Vitacolonna, E., ... & Mastropasqua, R. (2016). Neuroretinal alterations in the early stages of diabetic retinopathy in patients with type 2 diabetes mellitus. *Eye*, 30(5), 673-679.
  19. Oshitari, T., Hanawa, K., & Adachi-Usami, E. (2009). Changes of macular and RNFL thicknesses measured by Stratus OCT in patients with early stage diabetes. *Eye*, 23(4), 884-889.
  20. Firat, P. G., Doganay, S., Demirel, E. E., & Colak, C. (2013). Comparison of ganglion cell and retinal nerve fiber layer thickness in primary open-angle glaucoma and normal tension glaucoma with spectral-domain OCT. *Graefes Archive for Clinical and Experimental Ophthalmology*, 251(3), 831-838.
  21. Ma, J., Zhang, Y., Zhu, T. P., & Xu, J. (2013). Correlation of optic retinal nerve fiber layer thickness and visual function in patients with nonproliferative diabetic retinopathy. [*Zhonghua yan ke za zhi*] *Chinese journal of ophthalmology*, 49(6), 514-520.
  22. Rodrigues, E. B., Urias, M. G., Penha, F. M., Badaró, E., Novais, E., Meirelles, R., & Farah, M. E. (2015). Diabetes induces changes in neuroretina before retinal vessels: a spectral-domain optical coherence tomography study. *International journal of retina and vitreous*, 1(1), 4.
  23. Funatsu, H., Yamashita, H., Ohashi, Y., & Ishigaki, T. (1992). Effect of rapid glycemic control on progression of diabetic retinopathy. *Japanese journal of ophthalmology*, 36(3), 356-367.
  24. Nor-Sharina, Y., Zunaina, E., Shatriah, I., Win-Mar, K., & Azriani, A. R. (2013). Correlation of retinal nerve fibre layer thickness with HbA1c and oxidised LDL in non-proliferative diabetic Retinopathy. *J Diabetes Metab*, 4(298), 2.