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Original Research Article

Comparative Analysis of Retinal Nerve Fiber Layer Thickness in Patients of Primary Open Angle Glaucoma, Type 2 Diabetes Mellitus, and Primary Open Angle Glaucoma Having Type 2 Diabetes Mellitus

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Abstract

Retinal nerve fiber layer thickness (RNFLT) is affected in several ocular and systemic conditions, most commonly glaucoma and diabetic retinopathy. This cross sectional study was done to compare the RNFLT in 180 eyes of 90 patients. A total of 90 patients were assigned to 3 groups of 30 patients each of primary open angle glaucoma (POAG), type 2 diabetes mellitus (T2DM) and POAG with T2DM (POAG/T2DM). The RNFLT was measured with spectral-domain OCT. Readings from all the areas of retina were measured in both eyes. Presence of T2DM in patients of POAG significantly affected the RNFLT as compared to patients of POAG or T2DM individually. The RNFLT was 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 POAG/T2 DM. The changes in RNFLT can be used to monitor the progression of diseases affecting RNFLT and efficacy of treatment modalities.

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

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 several ocular and systemic conditions, most commonly glaucoma and diabetic retinopathy. 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 [2, 3]. The POAG is the most common form of glaucoma. Retinal nerve fiber loss precedes measurable ONH changes and visual field defects [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 [3]. There are various techniques, such as confocal scanning laser polarimetry (GDX with variable corneal compensation) and Optical coherence tomography (OCT), which helps in quantitative, reproducible and objective measurement of ONH and RNFLT [3].

Diabetes mellitus is a metabolic disorder. The type 2 Diabetes mellitus (T2DM) is more common than type 1. Diabetic complications include microvascular complications such as retinopathy, nephropathy and neuropathy apart from macrovascular complications. In addition to vascular changes, the earlier stages of DR

cause neurodegenerative changes such as loss of RGC, glial cell reactivity and thinning of RNFL [4, 5]. Moreover, 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 [5-7]. Spectral-domain OCT (SD-OCT) has been used to show that RNFL thinning in DR is due to RGC loss [5-7].

Attempts have been made to find the correlations between thinning of RNFL and age, sex, duration of POAG and status of intraocular pressure (IOP) 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. Few authors who studied RNFLT in patients of POAG/T2DM have reported contradicting results [8-10]. But none has compared the RNFLT in the three groups. Further, no study in the past compared relationship of RNFLT and blood glucose levels. Hence, this study was carried out to evaluate the effect of POAG on RNFLT in patients of POAG/T2DM and compare it with patients having only T2DM and patients having only POAG and also find the correlation between blood glucose levels.

MATERIALS AND METHODS

The present cross sectional study was carried out on 90 patients in a Regional Institute of Ophthalmology in northern India. These patients were divided in three groups of 30 patients each having POAG, T2DM, and patients of POAG with T2DM, respectively. All patients had best corrected visual acuity (BCVA) of 6/12 or better, and open anterior chamber angles.

The following inclusion and exclusion criteria were applied respectively: In group I, patients of POAG having any two of the following characteristics for 1-3 year were included: i) IOP > 21 mmHg (without treatment), or < 21 mmHg (on anti-glaucoma treatment); ii) Glaucomatous field defects; iii) Glaucomatous ONH changes. Patients having history of diabetes mellitus were excluded from this group.

In group II, patients of T2DM having the any of following characteristics for more than 5 years were included: blood glucose levels ≥ 126 mg/dl (fasting) or ≥ 200 mg/dl (post prandial) according to ADA. The patients having intraocular pressure > 21 mmHg (without treatment) or <21 mmHg (on anti-glaucoma treatment); or glaucomatous field changes; or glaucomatous disc changes, were excluded from this group

In group III, patients of POAG having T2DM having any two of the following characteristic for 1-3 years were included: i) IOP > 21 mmHg (without treatment) or < 21 mmHg (on anti-glaucoma treatment); ii) Glaucomatous field defects; iii) Glaucomatous disc changes; and having any of the following characteristics for more than 5 years: iv) blood glucose levels ≥ 126 mg/dl (fasting) or ≥ 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 raised IOP, any other retinal diseases except DR, any kind of laser fundus photocoagulation in the past, high myopia, previous refractory or major intraocular surgery, corneal opacity and dense cataract.

A detailed history was taken and BCVA was noted. Then, slit lamp examination of anterior segment, Goldman- applanation tonometry, gonioscopy, visual field analysis using Humphry visual field analyser, dilated fundus examination using direct and indirect ophthalmoscopy and biomicroscopy of the posterior segment using +90 D lens were done.

Optical coherence tomography was done on spectral-domain 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. Three 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. The RNFLT was also calculated for all 16 sectors of RNFL.

The data was entered in Microsoft excel spreadsheet and statistically analysed using SPSS (Statistical Package for the Social Sciences) software version 21.0 (SPSS Inc., Chicago, IL.). Clinical data

was expressed as mean ± standard deviation (SD) and percentage (%). The difference was considered statistically significant when the p value was < 0.05.

RESULTS AND DISCUSSION

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

Table-1: Age Distribution of cases

Age-range (years)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (POAG+T2DM) (n=30)
<30	1	0	0
31-40	2	4	0
41-50	6	7	4
51-60	8	11	10
>60	13	8	16
Mean ±SD	56.6 ± 11.5	54.1 ± 9.8	61.1 ± 8.3

On statistical analysis, the difference between only groups II and III was significant

(p = 0.003). More patients were in older age-range in group III.

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

Table-2: Sex distribution of cases

Sex	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (POAG+T2DM) (n=30)
Male	14 (46.70%)	16 (53.30%)	15 (50%)
Female	16 (53.30%)	14 (46.70%)	15 (50%)

On statistical analysis, sex ratio was comparable in the three groups.

The mean durations of POAG in groups I and III were as shown in Table-3.

Table-3: Mean duration of POAG

Duration (years)	Group I (POAG) (n=30)	Group III (POAG+T2DM) (n=30)	P value I vs. III
Mean ± SD	2.14 ± 0.75	2.03 ± 0.85	0.636 NS

vs. = versus; NS = Not significant

The mean duration of POAG was comparable between group I and III.

The mean durations of DM in group II and III were as depicted in table 4.

Table-4: Mean duration of DM

Duration (years)	Group II (T2DM) (n=30)	Group III (POAG+T2DM) (n=30)	P value II vs. III
Mean ± SD	9.40 ± 4.47	9.93 ± 4.27	0.640 NS

Duration of diabetes was comparable between group II and III, and thus insignificant.

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

Table-5: Routine laboratory investigations for Type 2 DM

Investigations	Group II (T2DM) (mean ± SD)	Group III (POAG+ T2DM) (mean ± SD)	P value II vs. III
Fasting plasma glucose (mg/dl)	147.96 ± 34.90	166 ± 4081	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

Sig.=Significant; NS= Not significant

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

The various microvascular complications of DM include DR, diabetic nephropathy and diabetic neuropathy; and macrovascular complications such as stroke, coronary artery disease and peripheral arterial disease were noted in group II and III (Table-6).

Table-6: Various diabetic complications in group II and III

Complications	Group II (T2DM) (n=30)	Group III (T2DM + POAG) (n=30)	P value II Vs. III
Microvascular	23 (76.70%)	24 (80%)	0.754 NS
Macrovascular	9 (30%)	12 (40%)	0.416 NS

Microvascular and macrovascuar complications of diabetes were present in large number of cases in group II and III, but this was not significantly different between the two groups.

The RNFLT of right eye in different areas was as shown below.

Table-7: Mean superior nasal RNFLT of RE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM+POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Superior nasal RNFLT	99.9±17.5	113.1±21.5	96.2±16.3	0.01 Sig.	0.001 Sig.	0.401 NS

On statistical analysis, the differences between groups I vs. II, and II vs. III were found to be significant.

Table-8: Mean nasal upper RNFLT of RE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM +POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Nasal upper RNFLT	72.9±15.2	77.0±12.8	64.0±16.5	0.264 NS	0,001 Sig.	0.003 Sig.

On analysis, the differences between groups II vs. III, and I vs. III were significant.

Table-9: Mean nasal lower RNFLT of RE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM + POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Inferior nasal RNFLT	101.6±22.6	124.3±21.7	110.1±29.7	0.002 Sig.	0.03 Sig.	0.216 NS

On analysis, the differences between groups I vs. II, and II vs. III, were significant.

Table-10: Mean inferior temporal RNFLT of RE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM+POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Inferior temporal RNFLT	126.6±32.7	143.9±27.0	126.5±32.9	0.02 Sig.	0.02 Sig.	0.990 NS

On analysis, the differences between groups I vs. II, and II vs. III, were significant.

Table-11: Mean temporal lower RNFLT of RE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM+POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Temporal lower RNFLT	75.6±18.1	77.3±14.3	70.06±17.7	0.642 NS	0.070 NS	0.230 NS

On statistical analysis, the differences amongst the three groups were found to be comparable, and thus insignificant.

Table-12: Mean temporal upper RNFLT of RE

Parameter (mean±SD) (µm)	Group 1 (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM+POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Temporal upper RNFLT	77.3±18.4	84.4±18.8	76.4±21.3	0.148 NS	0.131 NS	0.861 NS

On statistical analysis, the differences amongst the three groups were insignificant.

Table-13: Mean superior temporal RNFLT of RE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM+POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Superior temporal RNFLT	120.2±22.5	131.9±20.0	115.5±21.6	0.03 Sig.	0.003 Sig.	0.413 NS

On statistical analysis, the differences between groups I vs. II, and II vs. III were significant.

Table-14: Mean superior nasal RNFLT of LE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM + POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Superior nasal RNFLT	106.8±27.6	123.2±16.8	102.63±21.0	0.007 Sig.	0.001 Sig.	0.512 NS

On statistical analysis, the differences between groups I vs. II, and I vs. III, were significant.

Table-15: Mean nasal upper RNFLT of left eye

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM+ POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Nasal upper RNFLT	75.9±24.5	80.2±15.8	74.2±18.3	0.426 NS	0.179 NS	0.757 NS

On statistical analysis, the differences amongst the three groups were insignificant.

Table-16: Mean nasal lower RNFLT of LE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM + POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Nasal lower RNFLT	69.4±19.5	75.0±13.3	69.4±19.8	0.199 NS	0.209 NS	0.989 NS

On statistical analysis, the differences amongst the three groups were insignificant

Table-17: Mean inferior nasal RNFLT of LE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM + POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Inferior nasal RNFLT	116.9±31.6	134.2±22.2	121.6±32.8	0.01 Sig.	0.08 NS	0.571 NS

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

Table-18: Mean inferior temporal RNFLT of LE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM + POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Inferior temporal RNFLT	119.7±33.8	132.7±20.1	117.0±26.8	0.070	0.01 Sig.	0.739 NS

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

Table-19: Mean temporal lower RNFLT of LE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM + POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Temporal lower RNFLT	65.8±15.8	67.0±10.3	64.0±12.9	0.729 NS	0.329 NS	0.637 NS

On statistical analysis, the differences amongst the three groups were insignificant.

Table-20: Mean temporal upper RNFLT of LE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM + POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Temporal upper RNFLT	71.3±20.5	78.0±15.4	73.3±16.2	0.156 NS	0.247 NS	0.682

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

Table-21: Mean superior temporal RNFLT of LE

Parameter (mean±SD) (µm)	Group I (POAG) (n=30)	Group II (T2DM) (n=30)	Group III (T2DM + POAG) (n=30)	P value I vs. II	P value II vs. III	P value I vs. III
Superior temporal RNFLT	115.26±30.79	132.76±19.82	117.16±24.67	0.01 Sig.	0.001 Sig.	0.792 NS

On statistical analysis, the differences between groups I vs. II, and II vs. III, were significant.

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

Table-22: Correlation between duration of glaucoma and RNFL thickness RE and LE in group I

	RE			LE		
Parameter (mean±SD) (µm)	**R value**	**P value**	**Statistical Significance**	**R value**	**P value**	**Statistical Significance**
Superior nasal RNFLT	0.191	<0.05	Sig.	-0.339	>0.05	NS
Nasal upper RNFLT	0.042	<0.05	Sig.	-0.179	>0.05	NS
Nasal lower RNFLT	-0.025	<0.05	Sig.	-0.160	>0.05	NS
Inferior nasal RNFLT	-0.198	>0.05	NS	-0.347	>0.05	NS
Inferior temporal	-0.253	>0.05	NS	-0.494	<0.01	Sig.
Temporal lower RNFLT	-0.087	>0.05	NS	-0.480	<0.01	Sig.
Temporal upper RNFLT	-0.141	>0.05	NS	-0.450	<0.05	Sig.
Superior temporal RNFLT	0.028	>0.05	NS	-0.436	<0.05	Sig.

When correlated, the duration of glaucoma with the RNFLT of the RE in group I, superior nasal, nasal upper, nasal lower were negatively correlated and statistically significant (p<0.05). In the rest of the quadrants, RNFLT was negatively correlated but statistically insignificant (p>0.05). When compared in the LE, inferior temporal, temporal lower, temporal upper and superior temporal RNFLT was found to be negatively correlated and statistically significant (p <0.05).

The correlation between duration of DM and RNFLT of RE and LE in group II was analysed using Pearson's coefficient of correlation (Table-23).

Table-23: Correlation between duration of DM and RNFLT in RE and LE in group II

	RE			LE		
Parameter (mean±SD) (µm)	**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

When correlated, the duration of diabetes with RNFLT in group II, except for superior nasal, nasal upper and nasal lower sectors of RNFLT in the LE, all the other sectors of RNFLT in both eyes were negatively correlated but statistically insignificant (p>0.05).

The correlation between duration of DM and RNFLT of RE and LE of group III was analysed using Pearson's coefficient of correlation (Table-24).

Table-24: Correlation between duration of diabetes and RNFLT of RE and LE in group III

	RE			LE		
Parameter (mean±SD) (µm)	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 and LE in group III, all the sectors of RNFLT were found to be negatively correlated and statistically significant (p<0.01), except Inferior nasal RNFLT in LE, which was negatively correlated, but statistically insignificant (p >0.05).

The correlation between duration of POAG and RNFLT of RE and LE in group III was analysed using Pearson's coefficient of correlation (Table-25).

Table-25: Correlation between duration of glaucoma and RNFLT of RE and LE of group III

	RE			LE		
Parameter (mean±SD) (µm	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	Sig.	-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, the duration of glaucoma with RNFLT of RE in group III, only superior nasal, nasal lower, inferior temporal, temporal upper and superior temporal sectors of RNFLT were negatively correlated and statistically significant (p<0.050). When compared in the LE, only temporal upper and superior temporal sectors were negatively correlated and statistically significant. (<0.05).

The correlation between HbA1c and RNFLT of RE and LE in group II was analysed using Pearson' coefficient of correlation (Table-26).

Table-26: Correlation between HbA1c and RNFL thickness of RE and LE of group II

	RE			LE		
Parameter (mean±SD) (µm)	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	Sig.	0.070	>0.05	NS
Temporal upper RNFLT	-0.430	<0.01	Sig.	-0.183	>0.05	NS
Superior temporal RNFLT	-0.614	<0.01	Sig.	-0.310	>0.05	NS

When correlated, HbA1c with the RNFLT of RE in group II, only temporal lower, temporal upper and superior temporal sectors of RNFLT were negatively correlated and statistically significant ($p<0.01$). When similar comparison was made in the LE, superior nasal and nasal lower sectors were negatively correlated and statistically significant.

The correlation between HbA1c and RNFLT of RE and LE in group III was analysed using Pearson' coefficient of correlation (Table-27).

Table-27: Correlation between HbA1c and RNFL thickness of RE and LE of group III

	RE			LE		
Parameter (mean±SD) (µm)	R value	P value	Statistical Significance	R value	P value	Statistical Significance
Superior nasal RNFLT	-0.321	>0.05	NS	-0.435	<0.05	Sig.
Nasal upper RNFLT	-0.271	>0.05	NS	-0.437	<0.05	Sig.
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	Sig.
Temporal upper RNFLT	-0.382	<0.05	Sig.	-0.407	<0.05	Sig.
Superior temporal RNFLT	-0.335	>0.05	NS	-0.269	>0.05	NS

When correlated, HbA1c with RNFLT of RE in group III, only temporal upper RNFLT was found to be negatively correlated and statistically significant ($p<0.05$). When similar comparison was made in the left eye, superior nasal, nasal upper, temporal lower and temporal upper sectors of RNFLT were also negatively correlated and statistically significant ($p<0.05$).

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

DISCUSSION

Various studies have reported significant loss of RNFL in patients of POAG as well as in patients of type 2 DM [2-7]. And those, who studied RNFLT in patients of POAG/T2DM, have reported contrasting results [8-10]. But none has compared the RNFLT in the three groups. In the present study we evaluated the magnitude of decrease in RNFLT in patients of POAG, type 2 DM and patients of POAG with type 2 DM and compared the three groups.

In the present study, mean age of the patients was 56.6±11.5 years (range 30-70 years), 54.1±9.8 years (range 31-70 years) and 61.1±8.3 years (range 42-70 years) respectively, in group I, II and III. Age difference in the three groups was not statistically significant. Mean age in the present study was close to that reported by others [6, 7].

The sex ratio in the present study was comparable in the three groups with no statistically significant difference. It was similar to the results of the studies conducted by other investigators [7, 8].

Mean duration of diabetes in-group II and III was comparable. Some studies in the past found that RNFL thinning was accelerated by the progression of diabetic retinopathy [10]. In this study, the mean plasma glucose levels, both fasting and postprandial, in group III were higher than in group II, and this difference was statistically significant. Literature search showed, that no study in the past has evaluated the effect of blood glucose levels on RNFLT.

Duration of glaucoma was also similar in groups I and III. Hoyt et al. found that in glaucomatous eyes the RNFLT decreases with duration of glaucoma. [11]

In this study, it was observed that the patients having POAG/T2DM had statistically significant RNFL damage compared to those having POAG or T2DM only. The damage was more pronounced in superonasal quadrants, i.e. superior nasal and nasal upper; and inferotemporal quadrants, i.e. inferior temporal, temporal lower in the left eye while it was generalized in the right eye. To the best of our knowledge, no study in the past has compared RNFLT in patients of POAG, T2DM and POAG/T2DM. Several studies conducted in the past comparing RNFL thinning individually in the above three groups compared to the normal support the findings of the present study [7, 8, 12-14].

The observation of the present study regarding effect of POAG/T2DM on RNFLT is supported by Sari et al., who found that the RNFL was thinner in patients of POAG/T2DM compared to POAG and T2DM patients. Particularly, the superior quadrant was affected the most as in the present study [8]. Whereas, Akkaya *et al*., found that there was no significantly more thinning of RNFL in POAG/T2DM group as compared to the other two groups [9]. But, Hou *et al*., found a shielding effect of DM on RNFL thinning in POAG/T2DM group [10].

In the present study we found a negative correlation between duration of DM and RNFLT. Literature search showed that no study has been carried out in the past that gives the correlation between duration of diabetes and RNFL thinning. Similarly, we found a negative correlation between duration of glaucoma and RNFLT. Studies carried out by various investigators support our finding. [11, 16, 17]. We found a negative correlation between HbA1c and RNFLT. Nor- Sharina et al. conducted a cross sectional study and found no significant correlation between HbA1c and RNFLT [18]. Whereas, one study found that too rapid a decrease of HbA1c levels at the initiation of glycemic control could cause severe or transient exacerbation of the progression of retinopathy and worsening effect on RNFLT [19]. 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, longitudinal study with a larger sample size is required to monitor the effects glaucoma and glycemic control on RNFLT, to generalize the results.

CONCLUSION

We conclude that primary open angle glaucoma (POAG), and type 2 diabetes mellitus 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 POAG or DM individually. 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 of Ophthalmology*, 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 diabetic metabolic environment. *Annals of New York Academy of Science*, 1311, 174-190.
5. 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.
6. 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.
7. 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.
8. 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 of Scientific Research*, *6*(3), 31-34.
9. Akkaya, S., Can, E., & Öztürk, F. (2016). Comparison of the corneal biomechanical properties, optic nerve head topographic parameters, and retinal nerve fiber layer thickness measurements in diabetic and non-diabetic primary open-angle glaucoma. *International ophthalmology*, *36*(5), 727-736.
10. Hou, H., Shoji, T., Zangwill, L. M., Moghimi, S., Saunders, L. J., Hasenstab, K., ... & Penteado, R. C. (2018). Progression of primary open-angle glaucoma in diabetic and nondiabetic patients. *American journal of ophthalmology*, *189*, 1-9.
11. Hoyt, W. F., Schlicke, B., & Eckelhoff, R. J. (1972). Fundoscopic appearance of nerve- fiber-bundle defect. *British Journal of Ophthalmology*, *56*(8), 577-583.
12. Subbiah, S., Sankarnarayanan, S., Thomas, P. A., & Nelson Jesudasan, C. A. (2007). Comparative evaluation of optical coherence tomography in glaucomatous, ocular hypertension and normal eyes. *Indian Journal of Ophthalmology*, *55*(4), 283-287.
13. Firat, P. G., Doganay, S., Demirel, E. E., & Colac, 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 Archives of Clinical and Experimental Ophthalmology*, *251*(3), 831-838
14. 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.
15. Carpineto, P., Toto, L., Aloia, R., Ciciarelli, V., Borrelli, E., & Vitacolonna, E. (2016). Neuroretinal alterations in the early stages of diabetic retinopathy in patients with type 2 diabetes mellitus. *Eye (London)*, *30*(5), 673-679.
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. 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.
19. Funatsu, H., Yamashita, H., Ohashi, Y., & Ishigaki, Y. (1992). Effect of rapid glycemic control on progression of diabetic retinopathy. *Japanese Journal of Ophthalmology*, *36* (30), 356-367.