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Original Research Article

A comparison of macular ganglion cell complex thickness in diabetic patients with and without diabetic retinopathy using SD-OCT

Ravi Ranjan, Reena Sharma, Narendra Kumar Gupta, Himanshi Yadav*

Department of Ophthalmology, Uttar Pradesh University of Medical Sciences, Saifai, Etawah, Uttar Pradesh, India

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***Correspondence:**
Dr. Himanshi Yadav,
E-mail: himanshi76@gmail.com

ABSTRACT

Background: Diabetic retinopathy (DR) is a leading cause of visual impairment in working-age individuals. Retinal neurodegeneration due to pro-inflammatory cytokines and inflammation precede the clinical signs of DR. Preserving the integrity of the retinal ganglion cell (RGC) is essential for maintaining visual function.
Methods: This prospective, cross-sectional study involved 120 subjects, divided into three groups: 40 normal controls (G1), 40 diabetics without retinopathy (G2), and 40 diabetics with retinopathy (G3). Measurements of ganglion cell-inner plexiform layer (GC-IPL) and retinal nerve fibre layer (RNFL) thickness were taken for each participant. Data were analyzed using ANOVA and/or unpaired t-tests, and Pearson's correlation was used to evaluate the linear correlation between variables, with a significance threshold of $p<0.05$.
Results: The mean GC-IPL thickness was 84.81±5.02 µm for normal controls, 73.3±12.48 µm for diabetics without retinopathy, and 67.18±14.58 µm for diabetics with retinopathy (overall $p<0.001$). The mean RNFL thickness was 100.35±4.14 µm for normal controls, 85.80±14.04 µm for diabetics without retinopathy, and 80.25±21.03 µm for diabetics with retinopathy (overall $p<0.001$). There was no significant correlation between GC-IPL thickness and HbA1c levels ($p>0.05$).
Conclusions: Diabetic patients, both with and without DR, exhibited significant reductions in GC-IPL and RNFL thickness compared to controls, indicating neuro retinal changes precede vascular changes in DR. However, the correlation between RNFL/GC-IPL thickness and diabetes duration or HbA1c levels was not significant. Optical coherence tomography (OCT) is thus a useful non-invasive tool for early detection of neuronal loss before clinical signs of retinopathy.

Keywords: Diabetic retinopathy, Diabetic mellitus, GCL+IPL thickness, RNFL thickness, Spectral domain optical coherence tomography

INTRODUCTION

Diabetic retinopathy (DR) is the leading cause of visual impairment in the working age population and the most common ocular complication of diabetes mellitus (DM). Approximately 5% of diabetic eyes progress to severe visual acuity loss of 5/200 or less.[1,2] The ganglion cell complex (GCC) is defined as the three innermost retinal layers: the nerve fibre layer (RNFL), the ganglion cell layer (GCL), and the inner plexiform layer (IPL).[3] Retinal neurodegeneration due to pro-inflammatory cytokines and inflammation is suggested as an early event that precede the clinical signs of DR in diabetic patients.[4] The integrity of the retinal ganglion cell (RGC) is crucial for preserving visual function. RGC loss can be reflected in the reduction of the peripapillary RNFL or macular GCIPL complex thickness.[5] The high resolution of spectral domain OCT (SDOCT) allows detailed measurement of the thickness of individual retinal layers and may help demonstrate the early neurodegenerative effects of DM on inner retinal structures and optic disc.[6] The purpose of this study was to evaluate the thickness of GCC layer in patients with diabetic retinopathy and without diabetic retinopathy using SDOCT, and compare it with controls.

METHODS

This was a prospective, cross-sectional study of diabetic patients and controls. It was conducted in the Department of Ophthalmology of a tertiary care hospital from July 2021 to June 2022. Permission was obtained from the Institutional Ethical Committee of the University before commencing the study (The Ethical Clearance Number is 213/2020-21 dated 21/06/2021). Diabetic patients were recruited from OPD. The patient's data were collected including age, gender, duration of diabetes, medications used and any associated systemic illnesses. The examination included visual acuity for near and distance using logMAR chart, refractive correction, slit lamp examination, IOP (using Goldman applanation tonometer) and fundoscopy (using 90 D biomicroscope and indirect ophthalmoscope).

A total of 120 subjects above 40 years of age were recruited and divided into three groups, of which, 40 were normal controls (G1), 40 were diabetic without retinopathy (G2) and 40 were diabetic with retinopathy(G3). Only one eye of each subject was used for the SD-OCT analysis. Only one eye of each subject was used for the SD-OCT analysis. One eye of each patient (OD/OS) was selected by randomization, and GCC and retinal nerve fiber layer analysis was done using the Zeiss Cirrus HD-OCT model 500 (Germany). It was performed through a dilated pupil by the same operator each time. Macular scan was done using the macular cube 512×128 scan protocol. The GCA algorithm, incorporated into the Cirrus SD-OCT software was used to process and measure the thickness of the macular GC-IPL within a 14.13 mm^2 elliptical annulus area centred on the fovea. RNFL thickness was measured with the fast RNFL scanning protocol (256 A-scans). Only good-quality scans, defined as scans with signal strength ≥six, were used for the analysis. The patient was excluded if repeat scans were unsatisfactory.

Patients below the age of 40 years, history of previous ocular surgery/ trauma, intraocular injections or photocoagulation, macular oedema, presence of media opacities affecting the OCT examination, any high-risk proliferative diabetic retinopathy condition altering the OCT examination (i.e. preretinal haemorrhages, traction retinal detachment etc.) were excluded. The eyes with other retinal disorders affecting RNFL and GCC layers were also excluded.

The statistical analysis for this study was performed using the IBM Statistical Package for the Social Sciences (SPSS) version 20.0. Measurements were compared using ANOVA and/or unpaired t-test and Pearson's correlation was performed to evaluate the linear correlation between variables. A calculated p-value <0.05 was considered statistically significant.

RESULTS

We studied 120 eyes of 120 patients. The mean age of G1, G2 and G3 groups was 53.75±8.45,54±8.76 and 55.13±7.9years respectively (p-value 0.227). Most of subjects were in the age group of 51-60 years (42.50% diabetic with retinopathy, 37.50% diabetic without retinopathy, 45.00% normal control). There was no gender predilection (p-value 0.92, Table 1).

On fundus examination of DM patients, 21 eyes had mild non proliferative diabetic retinopathy (NPDR), 14 had moderate NPDR, 2 had severe NPDR and 3 patients had proliferative diabetic retinopathy (PDR).

Table 1: Baseline parameters of study groups.

Parameter	G1 (n=40)	G2 (n=40)	G3 (n=40)	P values			
				Overall	G1 vs. G2	G1 vs. G3	G2 vs. G3
Mean age (years)	53.75±8.45	54±8.6	55.13±7.9	0.448	0.44	0.227	0.274
Gender N (% male)	19 (47.50)	21 (52.50)	22 (55.00)	0.792	-	-	-
Duration of DM (years)	-	8.08±3.02	10.5±4.28	0.005	-	-	0.002
RBS (mg/dl)	101.35±11.83	204.9±60.79	222±65.22	<0.001	<0.001	<0.001	0.114
HbA1C (%)	5.23±0.32	8.09±1.38	8.97±1.54	<0.001	<0.001	<0.001	0.004
Mean BCVA (logMAR)	0.03±0.07	0.1±0.11	0.18±0.12	0.001	-	-	-

The mean HbA1c in Group 1, Group 2 and Group 3 was 5.23±0.32%, 8.09±1.38% and 8.97±1.54% respectively (p=<0.001). There was a significant difference between the mean value of HbA1c levels in the study groups. The duration of diabetes was shown to be significantly different between the two diabetic groups. The mean duration in G2 was 8.08±3.02 years and G3 was 10.5±4.28 years.

GC-IPL thickness (average as well as local) was significantly thinner in all diabetic patients (p=<0.001) compared to the control group. Additionally, further analysis in two diabetic groups showed that GC-IPL was thinner in DM with DR (p=<0.023) (Table 2).

Table 2: OCT macular ganglion cell complex thickness in study patients.

GCC thickness (µm)	Normal control	Diabetic without retinopathy	Diabetic with retinopathy	P values			
				Overall	G1 vs. G2	G1 vs. G3	G2 vs. G3
AGC-IPL	84.18±5.02	73.3±12.48	67.18±14.58	<0.001	<0.001	<0.001	0.023
SGC-IPL	85.03±4.7	73.25±14.93	63.9±16.77	<0.001	<0.001	<0.001	0.005
IGC-IPL	83.43±6	69.38±19.36	59.68±17.47	<0.001	<0.001	<0.001	0.011
MGC-IPL	81.03±6.42	58.23±21.52	39.58±18.57	<0.001	<0.001	<0.001	<0.001

Note- AGC-IPL= average GC-IPL, SGC-IPL= superior GC-IPL, IGC-IPL=inferior GC-IPL, MGC-IPL=minimum GC-IPL

Table 3: RNFL thickness (OCT) in diabetic patients and control.

RNFL thickness (µm)	Normal control	Diabetic without retinopathy	Diabetic with retinopathy	P values			
				Overall	G1 vs. G2	G1 vs. G3	G2 vs. G3
ARNFL	100.35±4.14	85.80±14.04	80.25±21.03	<0.001	<0.001	<0.001	0.084
SRNFL	128.93±9.62	107.95±20.5	124.55±182.93	<0.001	<0.001	<0.001	<0.001
IRNFL	130.05±7.9	106.83±22.91	93.70±30.36	<0.001	<0.001	<0.001	0.016
NRNFL	76.73±8.63	71.33±20.12	64.70±22.68	0.015	0.061	0.001	0.085
TRNFL	66.65±6.39	58.90±9.82	62.80±16.4	0.014	<0.001	0.085	0.100

Note-ARNFL=average RNFL, SRNFL=superior RNFL, IRNFL= inferior RNFL, NRNFL=nasal RNFL, TRNFL= temporal RNFL

Table 4: Relationship of OCT parameters with HbA1c and duration of diabetes.

GCC and RNFL thickness (µm)		HbA1c (%)				
		<6	**6.1 - 8.0**	**8.1 - 10.0**	**> 10.0**	**P value**
AGC-IPL	G1	84.13±5.08	86±0	-	-	0.718
	G2	76.00±0	71.38±14.7	76.09±9.24	76.50±3.32	0.714
	G3	-	70±14.62	64.2±15.22	70.3±13.36	0.445
ARNFL	G1	100.28±4.17	103±0	-	-	0.524
	G2	57.00±0	86.54±15.87	85.45±8.89	89.50±8.19	0.209
	G3		83.3±27.33	80.4±18.16	76.9±21.23	0.801
Duration of DM (years)						
		<5 years	5-10 years	> 10 years	P value	
AGC-IPL	G2	72±16.01	74.67±9.7	53±33.94	0.053	
	G3	66.5±31.82	67.04±13.95	67.5±14.67	0.994	
ARNFL	G2	83±5.32	87.27±14.11	69.5±23.33	0.193	
	G3	104±1.41	83.38±21.3	71.5±18.34	0.060	

Note- AGC-IPL= average GC-IPL, ARNFL=average RNFL

RNFL (average as well as local) was significantly thinner in all diabetic patients(p=<0.015). Also, the thinning of RNFL was more in superior and inferior quadrant in diabetic retinopathy eyes (p=<0.016) (Table 3).

Figure 1 and Figure 2 depicts the difference in OCT macular GCL-IPL thickness and OCT RNFL of control (a), diabetic without retinopathy (b) and diabetic with retinopathy (c) respectively.

There was no correlation between GCC thickness and HbA1c level (p>0.05).

As the duration of diabetes and HbA1c increases, there was no significant loss of GC-IPL and RNFL thickness (Table 4).

Superior GC-IPL was thinner in all diabetic patients with increasing duration of DM but was statistically significant only in diabetic retinopathy group. Nasal RNFL showed significant thinning with increasing duration of DM in diabetic patients with retinopathy.

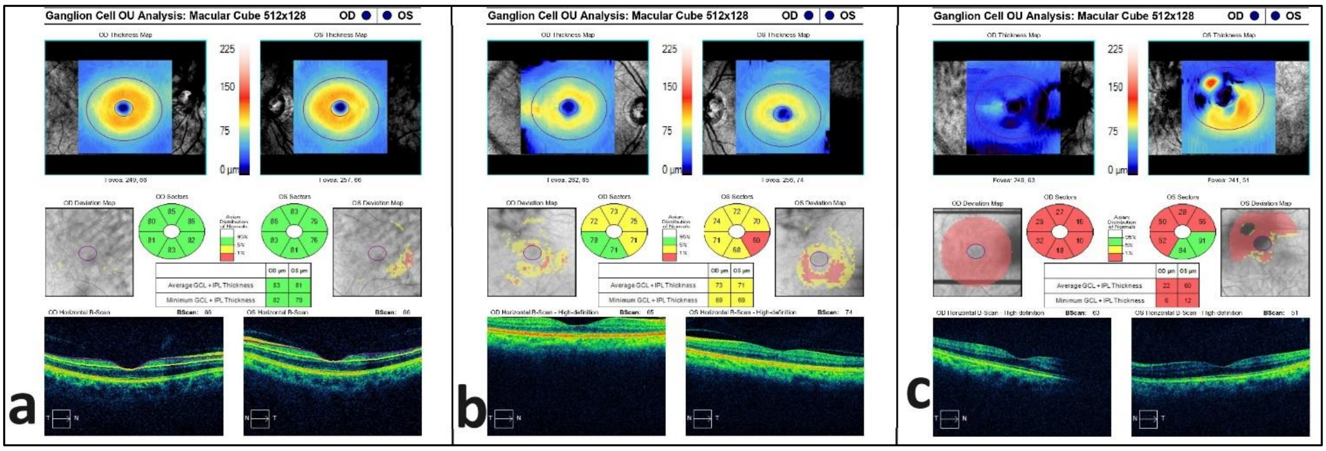

Figure 1: (a) OCT macular GCL-IPL thickness of control, (b) diabetic without retinopathy and (c) diabetic with retinopathy.

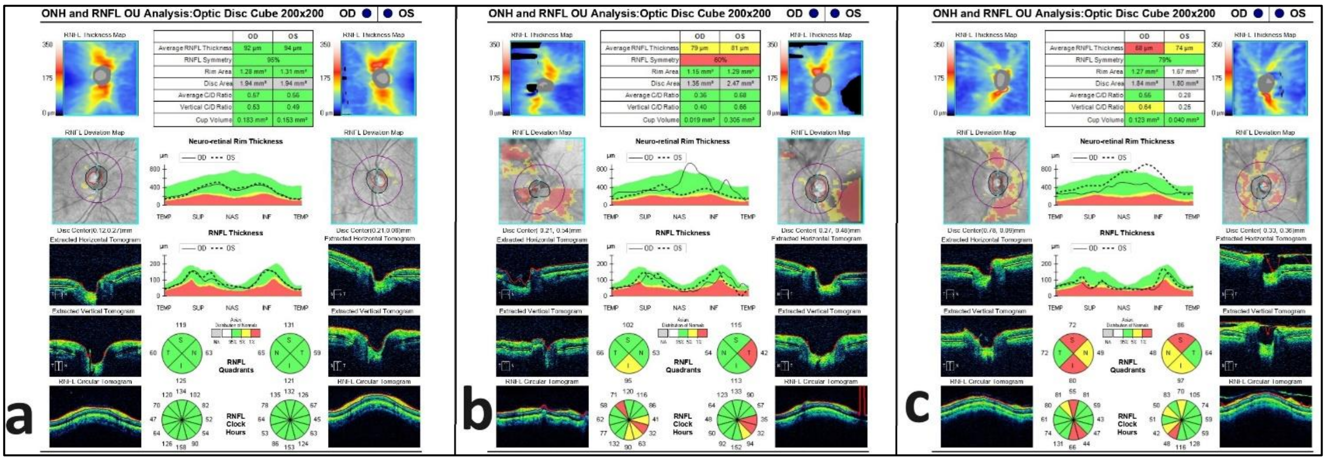

Figure 2: (a) OCT of RNFL of control, (b) diabetic without retinopathy and (c) diabetic with retinopathy.

DISCUSSION

Diabetic retinopathy remains a major cause of preventable blindness around the world. A good evaluation of the retinopathy can ensure early initiation of treatment and better final visual outcome. In this study using SD-OCT, the GC-IPL and RNFL thickness were evaluated in diabetic patients with and without DR.

Overall, the current analysis revealed a statistically significant reduction of the mean GC-IPL and mean RNFL thickness in diabetic patients compared with a homogenous control group (p value=<0.001). These findings were also present in diabetic patients without diabetic retinopathy compared with healthy controls, indicating this alteration occurs early in diabetes (p value=<0.001). The findings of the present study were consistent with the studies by Mehboob et al, Rodrigues EB et al and Carpineto et al who suggest neuroretinal changes occurring before the appearance of vascular signs of diabetic retinopathy.[7-9] This shows the early neurodegenerative changes and RGC loss in the retina. In our study, we found RNFL thickness in all the quadrants was reduced significantly in both diabetes groups compared with controls. The nasal quadrant RNFL was slower to change and was significantly thinner in diabetic retinopathy eyes compared to controls (p value=0.001). Nor-Sharina et al noticed that the thickest RNFL in nasal quadrant might be due to the lack of microaneurysm presence in this area and therefore less retinal nerve fibre layer damage occurred in this quadrant.[10] The published data is variable in the quadrants involved in RNFL thinning. Majority have reported thinning in superior and inferior quadrants.[11-13]

We also observed that there was statistically significant thinning of mean, superior, inferior and minimum GCL + IPL thickness in both diabetes groups compared to controls. Similar results are reported in diabetic patients in previous studies.[14-16]

Sugimoto et al found that glycaemic control (HbA1c levels) affects RNFL within 4 months.[17] Sahin et al showed that there is a mild negative correlation between HbA1c and average RNFL thickness and concluded that thinning of RNFL might be related with increased rates of atherosclerosis in patients with type 2 DM.[18] Evre et al noted that HbA1c and diabetes mellitus duration were not associated with any of the studied ocular parameters, except for a moderate correlation between binocular RNFL symmetry percentage and DM duration.[19] We did not find a significant correlation between RNFL/GCL-IPL thickness with diabetes duration and HbA1c value in diabetic patients. These results were also observed in studies done by Srinivasan et al and Chihara et al.[20,21]

CONCLUSION

In the present study, we have detected changes in the GC-IPL and the RNFL thickness by the SD-OCT in type 2 diabetic patients with and without DR. These changes may be related to both neuronal and vascular abnormalities that occur in the early stage of diabetic retina. The results of the study suggest that there was significant GC-IPL thinning and loss of RNFL in diabetics compared with healthy controls. AGC-IPL thickness was significantly thinner in diabetic patients with retinopathy while ARNFL thickness was similar. Superior GC-IPL was thinner in all diabetic patients with increasing duration of DM but was statistically significant only in diabetic patients without retinopathy. Nasal RNFL showed significant thinning with increasing duration of DM in diabetic patients with retinopathy. The GC-IPL and RNFL loss in diabetics could be an early indicator of neuronal loss. Hence OCT can be a useful non-invasive tool for early detection of neuronal loss even before retinopathy changes are seen.

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