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EARLY DETECTION OF CENTRAL VISION LOSS IN TYPE 2 DIABETES MELLITUS PATIENTS

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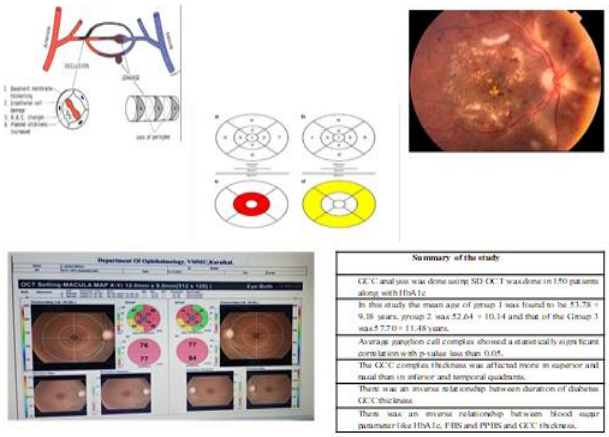
Abstract

Object: *The measurement of Ganglion Cell Complex in diabetic patients could be an early indicator of neuronal loss pointing to the central vision loss. In this study, we estimated the thickness of ganglion cell complex in Type-2 diabetic patients with or without retinopathy and observed the impact of diabetes on retinal ganglion cells.* ***Methodology:*** *After approval from our institutional ethical committee (VMMC/OPH/2019/01), this prospective study was conducted in the Department of Ophthalmology, Vinayaka Mission's Medical College, Karaikal. Totally 150 adult onset type 2 diabetic patients were recruited in the study. The study population was divided into 3 groups. Group 1- Normal healthy individuals, Group 2- Patients with Type-2 diabetes mellitus patients without diabetic retinopathy, Group 3- Patients with Type-2 diabetes mellitus patients with all grades (mild, moderate, severe) of Non proliferative retinopathy (According to ETDRS classification).* ***Results:*** *In this study the mean age of group I was found to be 53.78 + 9.18 years, group 2 was 52.64 + 10.14 and that of the Group 3 was 57.70 + 11.48 years. The average ganglion cell complex showed a statistically significant correlation in majority of sectors among the groups. The GCC complex thickness was affected more in superior than inferior sector. The nasal sector showed significant thinning of GGC than temporal. The duration of diabetes mellitus and the hyperglycemic level showed an inverse correlation to GCC thickness.* ***Conclusion:*** *This study noticed a significant GCC thinning in diabetic patients. Hence OCT can be a useful non-invasive tool for early detection of neuronal loss even before retinopathy changes are seen.*

Keywords: *Type 2 Diabetes Mellitus, Glycemic Status, Diabetic Retinopathy, OCT, Ganglion Cell Thickness.*

Pictorial Abstract



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INTRODUCTION

Type 2 Diabetes Mellitus (DM) is a prominent component of the metabolic syndrome and a primary cause of Indian ocular morbidity in the modern era. The measurement of GCC in diabetics using optical coherent tomography could be an early indicator of neuronal loss depicting the central vision loss. In this study, we estimated the thickness of ganglion cell complex in Type-2 diabetic patients with or without retinopathy and observed the impact of diabetes on retinal ganglion cells in comparison to the normal healthy control.

The retina is the innermost layer of the eyeball that runs from the optic disc to the Ora Serrata. Specifically, it is connected with visual functions and it transmits information to the visual cortex through the visual pathway. Due to the fact that it is metabolically active, it is very vulnerable to ischemia and nutritional deficiencies. Grossly retina can be divided into Optic disc, Macula lutea, equator and Ora serrata. The fovea centralis is a central depressed area of the macula that is situated in the centre of the eye and it is the most important part of the retina. It is completely composed of cones. The parafoveal area is made up of multiple layers of ganglion cells. The perifovea on the other hand symbolises the macula periphery where the number of ganglion cells is noticeably lesser than the central region.

The peripheral retina is thought to be positioned outside the temporal arcades where the ganglion cell layer is just a single layer thick. There are around 1.0-1.2 million axons of retinal ganglion cells present in the normal human optic nerve, all of which converge at the optic disc. These fibres together form the retinal nerve fibre layer and are responsible for vision.

Ganglion Cell Layer:

Ganglion cell layer is thicker at the macula measuring between 60 and 80 microns in diameter. The fovea is totally devoid of this layer of tissue. All visual information processed in the retina is collected by ganglion cells, which then transmits it to the brain. Ganglion cells can also be found in the inner nuclear layer or the inner plexiform layer.

The midget ganglion cells (P) are responsible for transmitting visual information from a single cone to another. Parasol ganglion cells (M type) are those that appear to receive input from all chromatic kinds of cone cells. M ganglion cells are activated in response to moving or changing stimuli and are responsible for transmitting this information to the brain. The ganglion cell complex (GCC) is composed of the three innermost retinal layers- the nerve fibre layer (neuron), the ganglion cell layer (ganglion cell layer), and the inner plexiform layer [1]

Prevalance of Diabetes Mellitus and Diabetic Retinopathy:

Insulin resistance is becoming an increasingly significant public health hazard. The World Health Organization projects that 578 million people will have diabetes by 2030, with the number growing by 51 percent (700 million) by 2045 [2]. Diabetic patients are expected to have a worldwide prevalence of any DR of 35.4 percent and PDR of 7.5 percent respectively. India has over 73 million diabetic patients with the number likely to climb to more than 123 million by 2040 according to current predictions.

Diabetic Retinopathy (DR) is found in 16.9% of the population in India with 3.6% incidence of sight threatening DR according to the results of the National Diabetes and Diabetic Retinopathy Survey (2015-19) [3]. Duration of Diabetes Mellitus, poor control of diabetes, associated hypertension, pregnancy, smoking, obesity and hyperlipidemia are identified to be the risk factors for diabetic retinopathy.

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Pathogenesis of Diabeic Retinopathy:

When glucose levels are elevated, the aldose reductase pathway transforms glucose into sorbitol which is then stored intracellularly. It is believed that the retinal vascular endothelium and pericytes experience osmotic damage as a result of the intracellular accumulation of this polyol which is irreversible. Hyperglycemia generated by diabetes result in the development of advanced glycation end products (AGEs) as a consequence of the non-enzymatic binding of glucose to the side chains of protein molecules. Accumulation of advanced glycation end products (AGE) in the retinal vasculature leads to the thickening of basement membrane and collapse of the blood retinal barrier [4]. VEGF-induced PKC activation occurs in phosphorylation of the tight junction protein which increases the permeability of the retinal vasculature and leads to the development of diabetic retinopathy. Glial cells play a crucial part in the proper functioning of neurons as well as the walls of blood vessels in the body by providing nutritional, immunological and protective functions of the neurons and blood vessels. Destruction of these cells as a consequence of diabetic complications is associated with a decline in visual function.

Early Treatment Diabetic Retinopathy Study (ETDRS) Classification:

I) Non-Proliferative Diabetic Retinopathy (NPDR) A. **Mild NPDR** At least one micro-aneurysm (MA), Definition not met for B, C, D, E and F. B. **Moderate NPDR** Haemorrhages, micro-aneurysms > Standard Photograph No. 2A, soft exudates, venous beading and Intra retinal micro-vascular abnormalities (IRMAs) definitely present. Definition not met for C, D, E and F. C. **Severe NPDR** (The 4:2:1 rule) Haemorrhages / MA in all 4 quadrants (> Standard photograph No.2A), Venous beading in 2 or more quadrants, IRMA in at least 1 quadrant (> Standard photograph No. 8A).

D. **Very Severe NPDR** Any two or more characteristics of severe NPDR; Definition not met for E, F. II) **Proliferative Diabetic Retinopathy (PDR):** (at least one of the following) 1. Neovascularization at disc (NVD) or neovascularization elsewhere (NVE), 2. Pre-retinal or vitreous haemorrhage, 3. Fibrous tissue proliferation.

High Risk PDR NVD >1/3-1/2 disc area or NVE > 1/2 disc area and pre-retinal or vitreous haemorrhage. III) **Advanced Diabetic Eye Disease:** It's a major vision-threatening complication of diabetic ketoacidosis that present with retinal traction bands or with retinal detachment. Vitreous haemorrhage and Neovascular Glaucoma are the other common complications of diabetic retinopathy due to new vessels.

Treatment:

Treatment includes lifestyle modification, control of blood sugar, hypertension and lipids. Intravitreal injections of anti-VEGF have been found to reduce macular edema and enhance vision in certain patients. They are ranibizumab, bevacizumab and aflibercept (VEGF Trap agent), Laser therapy is recommended for clinically significant macular edema in nonproliferative diabetic retinopathy. The leaking vessels are treated by focused laser photocoagulation right at the site of the leakage [5]. In circumstances when the leakage foci are not particular, a grid pattern of laser burns is used to seal the leakage. In the treatment of proliferative diabetic retinopathy (PDR), the process known as panretinal photocoagulation (PRP) is the main method of choice (PDR) [6]. Vitrectomy may be necessary in patients with longstanding vitreous haemorrhage and retinal detachment.

MATERIALS AND METHODS

After approval from our institutional ethical committee, this prospective study was conducted in the Department of Ophthalmology, Vinayaka Mission's Medical College, Karaikal. Patients were explained in their vernacular language and an informed consent was taken from all patients participated in this

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study. Totally 625 patients with adult onset diabetes were screened and 150 patients were recruited in the study.

Type 1 Diabetes Mellitus patients, any high risk proliferative diabetic retinopathy condition altering the OCT examination (i.e. preretinal hemorrhages, vitreous traction retinal detachment/combined retinal detachment), any other ocular disorders affecting GCC Layers. (Glaucoma, previous ocular surgeries, photocoagulation, diabetic macular edema, high myopia, severe ocular trauma) were excluded from the study.

The study population was divided into 3 groups. Group 1- Normal healthy individuals, Group 2- Patients with Type-2 diabetes mellitus patients without diabetic retinopathy, Group 3- Patients with Type-2 diabetes mellitus patients with all grades (mild, moderate, severe) of non-proliferative retinopathy (as per the ETDRS classification). A detailed history was recorded for all the patients. Complete Ophthalmic examination was done including best corrected visual acuity (BCVA), cycloplegic refraction, anterior and posterior segment evaluation using a slit lamp with biomicroscopy. FBS, PPBS and HbA1c were done and reports were collected.

GCC of all patients were evaluated using Nidek Spectral-Domain OCT machine. Comparison of all 3 groups was done by using the collected data. The OCT technique provides thickness information of the layer of interest. In Nidek OCT, a macular cube of 9 x 9 mm is scanned and analysis is performed on 6 or 9 mm with 128 B scans and 512 A scans resulting in three maps: a thickness map, a deviation map, and a thickness relative to a normative database map respectively.

The G Chart grid divides the macular area into eight areas. The mean thickness values of eight zones are shown by one grid, while the hemi superior and hemi inferior thicknesses are represented by another. It also features ETDRS sectors, which are used to compute and compare the mean regional thicknesses of the retinal layers.

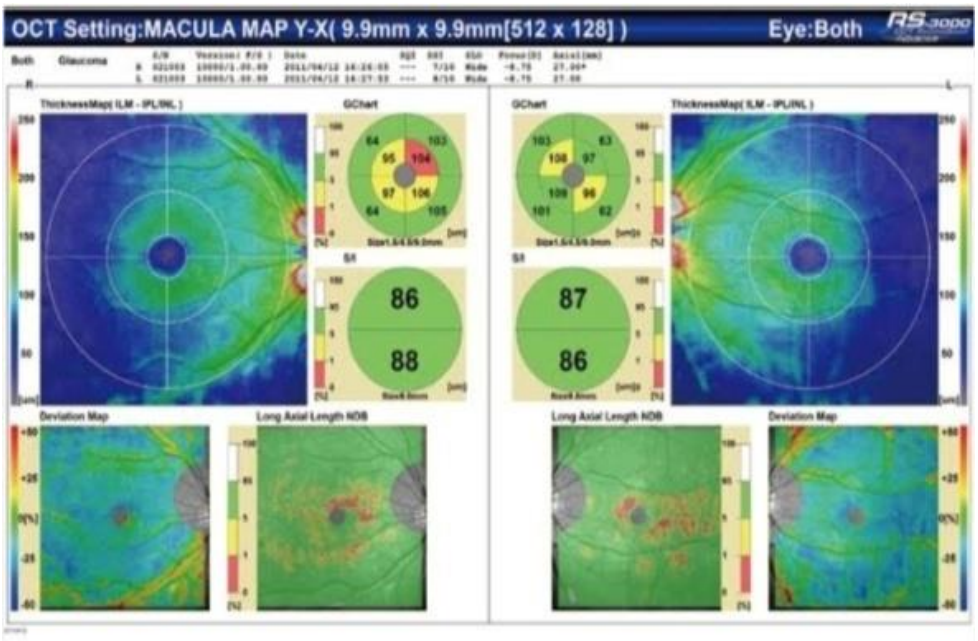

Figure 1: Macula Map (Both Eyes)

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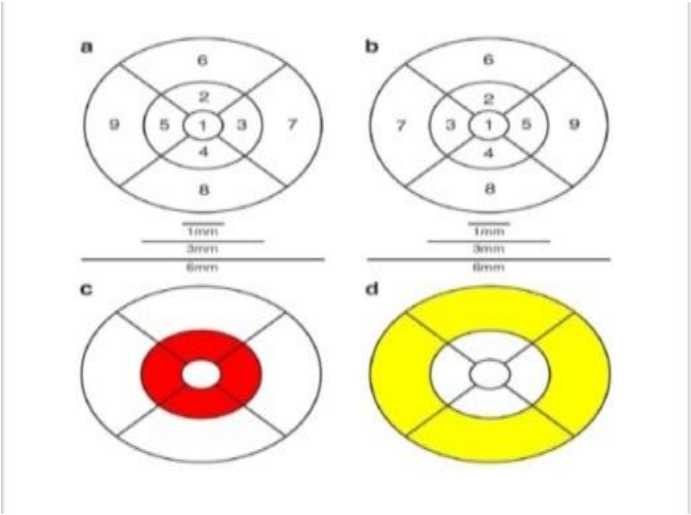

Figure 2: ETDRS Grid

Fig 2: (a) The right eye. (b) The left eye (c) By taking the average of the thickness measurements collected in each of the four quadrant locations (Red area), the thickness of the pericentral ring may be calculated. (d) The thickness of the yellow peripheral ring is the average of the four quadrant parts.

Descriptive and inferential statistical analysis was used to interpret the data. Continuous measurement data are displayed as Mean SD (Min-Max) whereas categorical measurement results are presented as Number (percentage). The significance was determined at a 5% level of significance. The significance of research parameters on a categorical scale between two or more groups was determined using the Pearson correlation co efficient to find the inverse relations.

RESULTS

Table 1: Age Distribution among Study Participants

Groups	Number	Mean± Std. Deviation
Group 1	50	53.78 + 9.18
Group 2	50	52.64 + 10.14
Group 3	50	57.70 +11.48
P value 0.036		

The mean age among the group 1 was 53.78 + 9.18 years, group 2 was 52.64 + 10.14 and that of the Group 3 was 57.70+11.48 years. The minimum age was 42 years in group 1, 40 years in group 2 and 42 years in group 3.The maximum age was 72 years in group1, 80 years in group 2 & 87 years in group 3.

Table 2: Gender Distribution among Study Participants

Sex	Group 1	Group 2	Group 3	Chisquare	df value	P value
Male	33(66%)	26(52%)	26(52%)	2.66	2	0.264
Female	17(34%)	24(48%)	24(48%)			
Total	50(100%)	50(100%)	50(100%)			

Majority of the participants were male which is 66% in group 1, 52% each in group2 and group 3. The distribution of sex was equal between the groups as shown by P value more than 0.05.

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Table 3: Comparison between Anterior segment findings among study participants

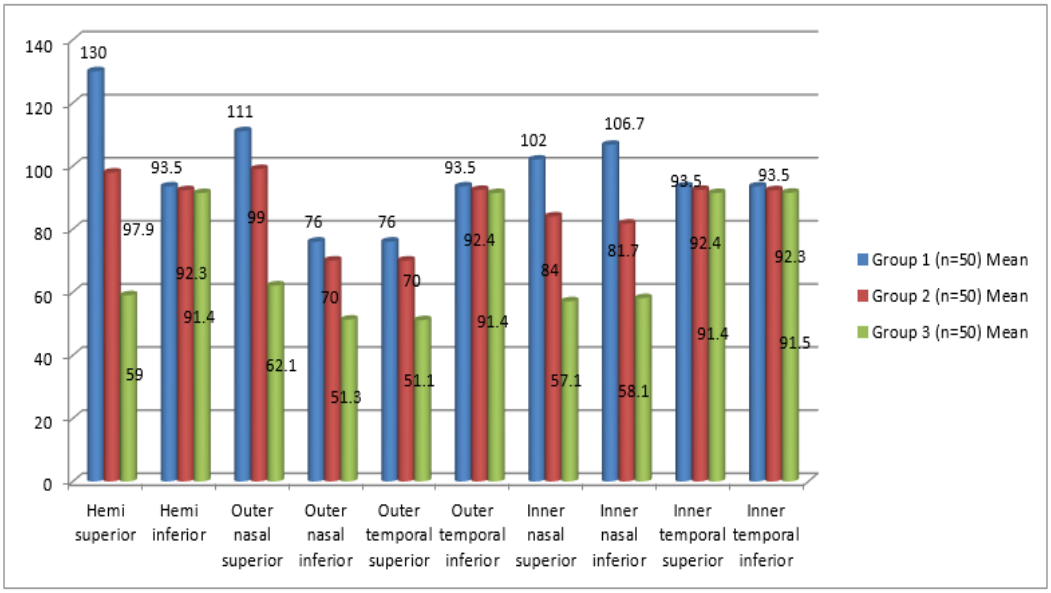
Anterior Segment	Group 1	Group 2	Group3	Total	Chisquare	df value	P value
Immature cataract	20(40%)	14(28%)	15(30%)	49(32.7%)	2.63	4	0.622
Normal	18(36%)	24(48%)	20(40%)	62(41.3%)			
Pseudophakia	12(24%)	12(24%)	15(30%)	39(26%)			

In anterior segment, majority of them had immature cataract which is 40% in group 1, 28% in group 2 and 30% in group 3. Pseudophakia was seen in 30% in group 3 and 24% each in both group1& 2. The distribution was insignificant between the groups as shown by P value more than 0.05.

Table 4: Distribution of HbA1C, FBS and PPBS among study participants

Groups	Number	HbA1C		FBS		PPBS	
		Mean	±Std. Deviation	Mean	±Std. Deviation	Mean	±Std. Deviation
Group 1	50	6.00	+0.00	94.88	+2.90	129.6	+6.44
Group 2	50	6.27	+0.44	133.12	+3.86	155.52	+20.64
Group 3	50	10.52	+1.90	167.80	+13.95	182.06	+14.84
P value 0.001							

Mean HbA1c level was 6.00+ 0.00 in group 1, 6.27 + 0.44 in group 2 and 10.52 + 1.90 in group3. Mean FBS level was 94.88+ 2.90 in group 1, 133.12 + 3.86 in group 2 and 167.80 + 13.95 in group 3. Mean PPBS level was 129.60 + 6.44 in group 1, 155.52 + 20.64 in group 2 and 182.06 +14.84 in group 3. All sugar values were high in group 3 when compared to other two groups with statistically significant p value of 0.001.



Graph 1: Distribution of OCT parameters among study participants

Above graph shows that the Hemi superior mean values in group 1, 2 and 3 were 130.0 + 4.1, 97.9 + 3.8 and 59.0 + 16.0 respectively. Hemi inferior mean values in group 1, 2 and 3 were 93.5 + 7.5, 92.3 + 9.6 and 91.4+8.6 respectively.

The Outer nasal superior mean values in group 1, 2 and 3 were 111.0 + 5.7, 99.0 + 2.4 and 62.1 + 13.1 respectively. The Outer temporal superior mean values in group 1, 2 and 3 were 76.0 + 4.3, 70.0 + 3.2 and 51.1 + 8.0 respectively. The Outer temporal superior mean values in group 1, 2 and 3 were 76.0 +

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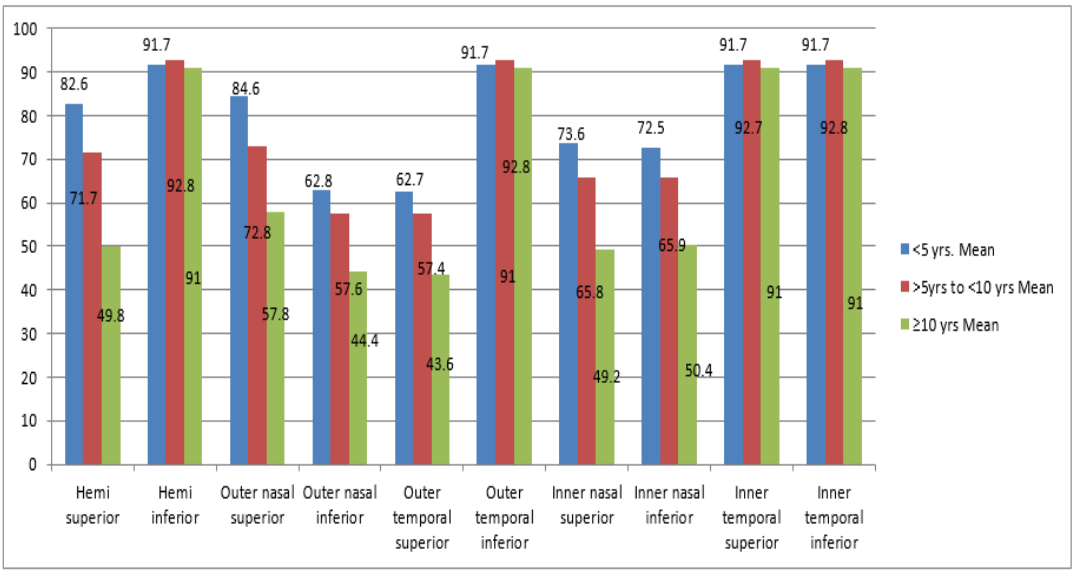
4.3, 70.0 + 3.2 and 51.1 + 8.0 respectively. The mean Outer temporal inferior value in group 1 was 93.5 + 7.5, group 2 was 92.4 + 9.6 and that of group 3 was 91.4 + 8.6.

The Inner Nasal Superior mean values in group 1, 2 and 3 were 102 + 2.2, 84.0 + 8.7 and 57.1 + 8.1 respectively. The Inner Nasal inferior mean values in group 1, 2 and 3 were 106.7 + 3.9, 81.7 + 8.1 and 58.1 + 7.8 respectively. Inner temporal superior mean values in group 1, 2 and 3 were 93.5 + 7.5, 92.4 + 9.6 and 91.4+8.6 respectively. In temporal inferior mean values in group 1, 2 and 3 were 93.5 + 7.5, 92.3 + 9.6 and 91.5 + 8.6 respectively.

The comparison of the mean distribution in hemi superior, outer nasal superior, outer nasal inferior, inner nasal superior, inner nasal inferior, outer temporal superior among the three groups was found to be significant with the p value less than 0.05 whereas the mean distribution of OCT parameters in hemi inferior, outer temporal inferior, inner temporal inferior, inner temporal inferior between three groups was insignificant with the p value more than 0.05.



Graph 2: Duration of Diabetes between OCT parameters among study participants

Above graph shows that the Hemi superior mean values in Diabetes groups <5 years, 5 to 10 years and >10 years were 82.6 + 21.0, 71.7 + 23.5 and 49.8 + 17.4 respectively and was found to be statisticaly significant with p value 0.001. Hemi inferior mean value in diabetic groups < 5 years, > 5 to < 10 years and >10 years were 91.7 + 9.2, 92.8 + 9.6 and 91.0 + 6.3 respectively. The Outer nasal superior mean values in diabetic groups < 5 years, > 5 to < 10 years and > 10 years were 84.6 + 18.7, 72.8 + 23.1 and 57.8 + 14.2 respectively.

The Outer nasal inferior mean values in diabetic groups < 5 years, > 5 to < 10 years and > 10 years are 62.8 + 10.2, 57.6 + 11.5 and 44.4 + 7.6 respectively. The mean values of the outer nasal sector among three groups were statistically significant with p value of 0.002 (outer nasal superior) and 0.001 (outer nasal inferior) respectively.

The Outer temporal superior mean values in diabetic groups < 5 years, > 5 to < 10 years and > 10 years were 62.7 + 10.2, 57.4 + 11.6 and 43.6 + 7.5 respectively with significant p value of 0.001. The mean Outer temporal inferior value in diabetic group < 5 years was 91.7 + 9.1, diabetic group > 5 to < 10 year was 92.8 + 9.7 and that of diabetic group > 10 years was 91.0 + 6.3 which was insignificant with p value 0.849.

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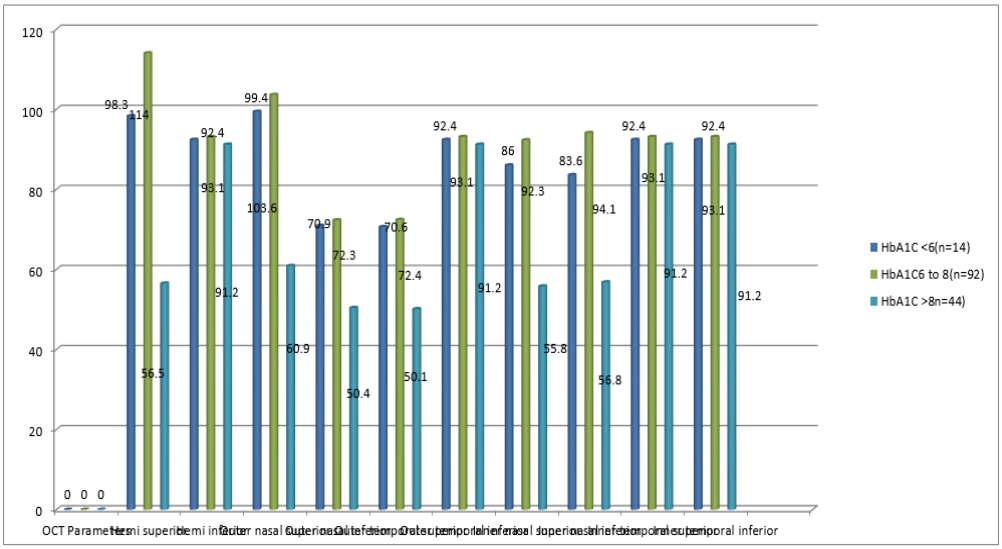
The Inner nasal superior mean values in diabetic groups < 5 years, > 5 to < 10 years and > 10 years were 73.6 + 14.8, 65.8 + 16.2 and 49.2 + 7.1 respectively The Inner nasal inferior mean values in diabetic groups < 5 years, > 5 to < 10 years and > 10 years were 72.5 + 13.3, 65.9 + 14.4 and 50.4 + 7.1 respectively. The mean values of inner nasal quadrants among three groups were statistically significant with p value of 0.001. Inner temporal Superior mean values in diabetic groups < 5 years, > 5 to < 10 years and > 10 years were 91.7 + 9.1, 92.7 + 9.6 and 91.0 + 6.3 respectively. Inner temporal inferior mean value in diabetic groups < 5 years, > 5 to < 10 years and > 10 years were 91.7 + 9.1, 92.8 + 9.6 and 91.0 + 6.3 respectively and was insignificant (p 0.865).



Graph 3: Distribution of HbA1c category ((<6, 6-8, >8) between OCT Parameters

Above graph shows that the Hemi superior mean values in HbA1c groups < 6, 6 to 8 and > 8 were 98.3± 3.5, 114.0 ± 19.1 and 56.5 ± 14.0 respectively. Hemi inferior mean value in HbA1c groups < 6, 6 to 8 and >8 were 92.4 + 7.4, 93.1± 8.8 and 91.2 ± 8.5 respectively.

The Outer nasal superior mean values in HbA1c groups < 6, 6 to 8 and > 8 were 99.4 ± 2.5, 103.6 ± 11.6 and 60.9 ± 13.2 respectively. The Outer nasal inferior mean values in HbA1c groups < 6, 6 to 8 and > 8 were 70.9± 4.0, 72.3 ± 7.1 and 50.4 ± 7.7 respectively.

The Outer temporal superior mean values in HbA1c groups < 6, 6 to 8 and > 8 were 70.6± 3.3, 72.4 ± 6.1 and 50.1 ± 8.0 respectively. The mean Outer temporal inferior value in HbA1c groups < 6 was 92.4 ± 7.4, HbA1c group 6 to 8 was 93.1± 8.8 and that of HbA1c group >8 was 91.2± 8.6.

The Inner Nasal Superior mean values in HbA1c groups < 6, 6 to 8 and >8 are 86.0 + 8.1, 92.3 ± 12.7 and 55.8 ± 7.7 respectively. The Inner Nasal inferior mean values in HbA1c groups < 6, 6 to 8 and >8 are 83.6 ± 7.7, 94.1 ± 15.4 and 56.8 ± 7.4 respectively.

Inner temporal superior mean value in HbA1c groups < 6, 6 to 8 and >8 was 92.4 ± 7.4, 93.1 + 8.8 and 91.2 ± 8.5 respectively. Inner temporal inferior mean value in HbA1c groups < 6, 6 to 8 and >8 were 92.4 ± 7.4, 93.1 + 8.8 and 91.2 ± 8.5 respectively.

The comparison of the mean of OCT parameters among three groups as per the HbA1C values in hemi superior, outer nasal superior, outer nasal inferior, inner nasal superior, inner nasal inferior, outer temporal superior sectors was found to be significant with the p value of 0.001. The p value was more than 0.05 in hemi inferior, outer temporal inferior, inner temporal inferior, inner temporal inferior sectors.

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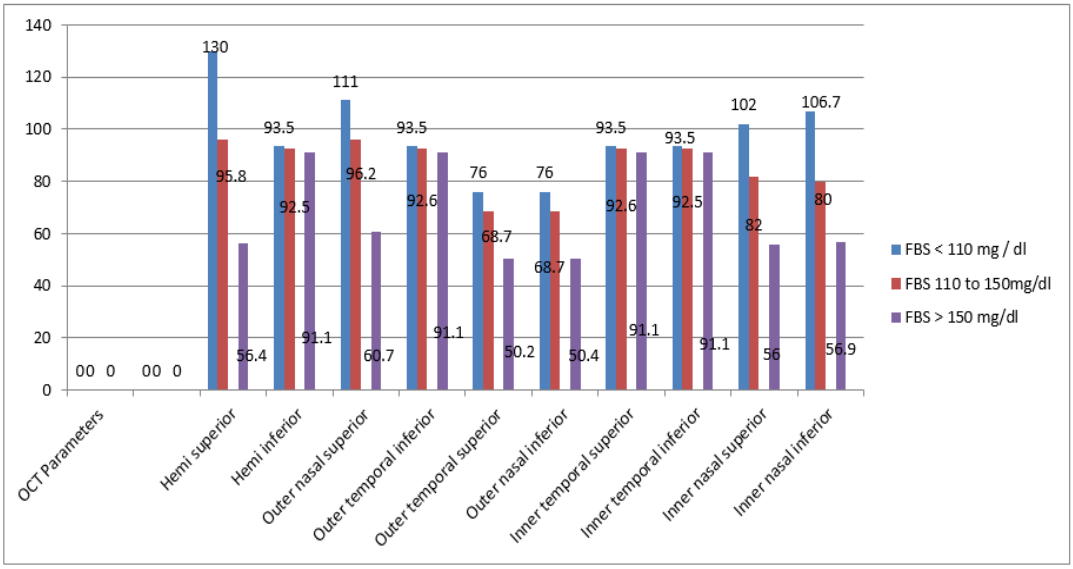

Graph 4: Distribution of FBS Category (<110, 110-150, >150) between OCT Parameters

The comparison of the mean of OCT parameters among three groups as per their FBS values in hemi superior, outer nasal superior, outer nasal inferior, inner nasal superior, inner nasal inferior, outer temporal superior sectors was found to be significant with the p value of 0.001. The p value was insignificant in hemi inferior, outer temporal inferior, inner temporal inferior, inner temporal inferior sectors.

Table 5: Distribution of PPBS category (<140,140-200,>200) between OCT parameters

OCT Parameters	PPBS<140 mg/ dl (n =51)		PPBS141-200mg/dl (n =93)		PPBS>200mg/dl (n =6)		F value	P value
	Mean	±SD	Mean	±SD	Mean	±SD		
Hemi superior	129.4	5.9	80.5	21.3	43.0	12.4	158.6	0.001
Hemi inferior	93.7	7.5	91.5	9.2	95.2	6.3	1.4	0.255
Outer nasal superior	110.8	5.8	82.6	19.4	46.0	1.3	78.4	0.001
Outer temporal inferior	93.7	7.5	91.6	9.2	95.2	6.3	1.4	0.262
Outer temporal superior	76.0	4.2	61.8	10.0	38.3	3.7	81.6	0.001
Outer nasal inferior	76.0	6.0	61.9	10.0	39.0	3.6	73.0	0.001
Inner temporal superior	93.7	7.5	91.6	9.2	95.2	6.3	1.4	0.259
Inner temporal inferior	93.7	7.5	91.6	9.2	95.2	6.3	1.3	0.264
Inner nasal superior	101.8	2.6	72.0	14.9	45.2	2.5	132.0	0.001
Inner nasal inferior	106.4	4.5	71.2	13.3	46.5	2.7	207.8	0.001

Comparison of the mean OCT parameters among three groups according to their PPBS values was found to be significant in hemi superior, outer nasal superior, outer nasal inferior, inner nasal superior, inner nasal inferior, outer temporal superior sectors with p value of 0.001 and was insignificant in the hemi inferior, outer temporal inferior, inner temporal inferior, inner temporal inferior quadrants.

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Table 6: Comparison between severity of Diabetic Retinopathy and OCT parameters

OCT Parameters	DR Mild (n = 17)		DR Moderate (n=17)		DR Severe (n=16)		F value	P Value
	Mean	±SD	Mean	±SD	Mean	±SD		
Hemi superior	74.0	9.6	56.4	13.9	45.9	9.2	27.0	0.001
Hemi inferior	90.0	9.7	91.0	9.4	93.4	6.3	0.7	0.509
Outer nasal superior	78.2	5.6	58.2	4.1	49.1	4.0	171.2	0.001
Outer temporal inferior	90.1	9.9	91.0	9.4	93.4	6.2	0.6	0.535
Outer temporal superior	57.9	1.7	53.6	4.3	41.2	4.5	90.0	0.001
Outer nasal inferior	57.8	1.4	53.5	4.6	42.0	4.6	74.5	0.001
Inner temporal superior	90.0	9.7	91.0	9.3	93.4	6.3	0.7	0.507
Inner temporal inferior	90.1	9.6	91.0	9.4	93.4	6.3	0.7	0.516
Inner nasal superior	65.0	3.0	57.2	3.2	47.7	3.3	132.5	0.001
Inner nasal inferior	66.4	3.2	58.3	3.1	49.0	3.3	120.5	0.001

Among the diabetic patients with retinopathy, the above table shows that there is progressive thinning of GCC as the severity of retinopathy increases in the hemi superior, inner and outer nasal sectors and also in outer temporal superior sector.

Table 7: Correlation between HbA1C, FBS, PPBS, Duration of DM and OCT Parameters

OCT Parameters	HbA1C		FBS		PPBS		Duration of DM	
	r	p	r	P	R	p value	R	p value
Hemi superior	-0.80	0.001	-0.96	0.001	-0.84	0.001	-0.69	0.001
Hemi inferior	-0.07	0.364	0.09	0.280	-0.10	0.219	-0.08	0.293
Temporal	-0.58	0.001	-0.64	0.001	-0.58	0.001	-0.46	0.001
Nasal	-0.82	0.001	-0.95	0.001	-0.85	0.001	-0.69	0.001
Outer	-0.83	0.001	-0.90	0.001	-0.81	0.001	-0.63	0.001
Inner	-0.73	0.001	-0.88	0.001	-0.79	0.001	-0.66	0.001

The above table shows that when there is increased duration of diabetes and with the elevated blood sugar levels, there is significant thinning of GCC in almost all sectors studied.

DISCUSSION

In this study, the duration of diabetes was significantly correlated with GCC thinning in the subjects which was comparable to the study conducted by Araszkiewicz A et al [7] which proved significant correlation among duration of diabetes, GCL thickness and neurological degeneration in diabetic retinopathy. However, in the study conducted by Chhablani J et al [8], no significant relationship was found between GCIPL and RNFL thicknesses and duration of diabetes. In Sankha Subhra Chaudhari et al [9] study, GCL thickness of the right and left eyes were found to be significantly reduced with the increased duration of diabetes which was similar to our study.

This study showed inverse correlation between HbA1c and GCC thickness which was comparable to the study conducted by MD Maria E.A Mikhail et al [10]. They also proved that there was a statistically significant correlation between thinning of most of RNFL and GCC quadrants and HbA1c level more than 9%. Similarly, in a study done by Mehmet Demir et al [11], characteristic GCC thinning was proved with higher HbA1c level in patients with DM compared to the controls. However, contrast to our study, the correlation of average RNFL thickness and GCL-IPL thickness in type 2 diabetic patients was not statistically significant with the duration of diabetes and HbA1c values in Mitali Borooah et al [12] study.

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In this study, both FBS and PPBS values showed an inverse correlation to GCC thinning in diabetic retinopathy patients which was similar to the study done by Debadatta Chakrabarty et al [13]. OCT parameters had significant correlation with blood glycemic parameters in diabetic patients with Pearson correlation coefficient analysis.

This study showed significant GCC thinning in diabetic patients in most of quadrants like hemi superior, outer and inner nasal sectors and in outer temporal superior quadrant which was similar to study conducted by Lim H.B et al [14]. In this study, only hemi superior GCC thickness was found to be significantly correlated among the 3 groups of patients which match with the study conducted by Hegazy AI et al [15]. In Mário Pincelli Netto et al study also [16], regional analysis of mean superior and inferior macular GCC showed significant thinning of GGC in superior macular region when compared to inferior region. The study done by Araszkiewicz A et a [7] compared type 2 diabetic patients with and without retinopathy and found thinning of GCC in both superior GCL (P =0.05) and inferior GCL (P = 0.006). In a study by Mehmet Demir etal[11] there was significant thinning in GCC but no statistical significance was found between superior and inferior whereas our study showed significant thinning in the superior quadrant.

In a study done by Gundogan FC et al [17], the outer temporal superior and outer temporal inferior sectors of macula showed significant thinning of GCC in diabetic patients ($p < 0.05$) while this study showed significant result only in superior (outer temporal) sector. In a study by Eduardo Büchele Rodrigues et al [18], sectoral analysis of GCL+ IPL showed a statistically significant difference in the following sectors: nasal inferior, nasal superior, hemi superior and hemi inferior. This study also shows the same except for the hemi inferior region. The study by Toshiyuki Oshitari et al [19] done with Fourier Domain OCT showed significant macular map in outer nasal and temporal superior more than inferior with respect to HbA1c and duration of diabetes similar to this study. The study done by Xia Gong et al [20] showed significant thinning of macular GC-IPL and GCC thickness in every gird of the macula.

CONCLUSION

This study noticed a significant GCC thinning in diabetic patients. 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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