ORIGINAL ARTICLE

Assessment of Retinal Ganglion-cell Complex in Diabetic Patients without Retinopathy Using Spectral-Domain Optical Coherence Tomography

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Abstract

Background: ***Microvascular alterations make up diabetic retinopathy (DR), but new research shows that neurodegeneration can start sooner. The original optical coherence tomography (OCT) system has undergone significant development since its introduction.***

Aim and objectives: ***The purpose of this study is to evaluate diabetic patients free of retinopathy by spectral domain optical coherence tomography of the ganglion cell complex.***

Subjects and methods: ***Between April and October of 2024, researchers at the Ophthalmology department of Al-Azhar University Hospitals performed a cross-sectional comparison study on 30 pairs of eyes: 30 healthy controls and 30 diabetes patients without retinopathy (group-B).***

Results: ***Compared to healthy controls, diabetic individuals without retinopathy had thinner macular GCL-IPL and RNFL thickness. Researchers observed a statistically significant relationship between the length of time a diabetic patient has had the disease, hemoglobin A1c, average RNFL thickness, and average GCL-IPL thickness.***

Conclusion: ***Patients with diabetes who do not have retinopathy had much thinner GCL-IPL and RNFL layers than the control group, suggesting that neurodegenerative alterations brought on by DM occur before vascular abnormalities associated with diabetic retinopathy manifest.***

Keywords: SD-OCT; OCT; Diabetic patients

1. Introduction

Diabetic retinopathy (DR) is the principal cause of blindness in people of working age, and diabetes mellitus (DM) is a rapidly increasing global epidemic that causes a lot of harm.[1]

The prevalence of DR has been on the rise. A third of those with DM also show signs of DR, according to recent estimates, which puts the global DM population at around 486 million. Hypertension, length of diabetes, diabetic neuropathy, diabetic nephropathy, fasting blood glucose, serum total cholesterol, serum triglycerides, and hemoglobin A1c are some of the risk factors for diabetic retinopathy (DR), a complex illness with multiple causes.[2]

The classic view of DR has focused on it as a microvascular disease with retinal microaneurysms, capillary changes, and hemorrhages as its primary symptoms. As the disease advances, these changes in blood vessel function may cause the inner retina's neuronal and glial components to degenerate. Nevertheless, new research indicates that microvascular alterations are not detectable until after retinal neurodegeneration has progressed.[3]

It appears that neurodegeneration in DM is a macula-wide process that causes functional problems like impaired color discrimination, decreased contrast sensitivity, and impaired dark adaptation.[1]

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An important step in the development of DR starts and activates a number of metabolic processes that contribute to microangiopathy and the breaking of the blood-retinal barrier.[4]

The retinal ganglion cells (RGCs) undergo the most rapid cell death and are the first to be damaged. Each of the three layers of the retina is made up of different types of retinal ganglion cells: the inner plexiform layer (IPL), the ganglion-cell layer (GCL), and the retinal nerve-fiber layer (RNFL).[5]

This study set out to evaluate diabetic patients free of retinopathy by use of spectral domain optical coherence tomography (OCT) in order to determine the thickness of the ganglion cell complex.

2. Patients and methods

Between April and October of 2024, researchers at the Ophthalmology department of Al-Azhar University Hospitals performed a cross-sectional comparison study on 30 pairs of eyes: 30 healthy controls and 30 diabetes patients without retinopathy (group B).

Inclusion criteria:

Age:18 years or older, and type-1 DM and type-2 DM.

Exclusion criteria:

The following conditions can impair OCT signals: diabetic retinopathy (DR), glaucoma, uveitis, prior ocular surgery, trauma, intraocular injections, laser photocoagulation, high refractive errors (myopia >-6.00 D or hypermetropia >+4.00 D), and substantial media opacity.

Study procedure:

The individuals who were part of the study and had recorded glucose levels (fasting plasma glucose level <100 mg/dL or hemoglobin A1c level <5.7% of total hemoglobin) were placed in the control group. These individuals came to our clinic for a variety of reasons, including health screenings and routine checks for eye diseases like cataracts and peripheral vitreous floaters. The individuals placed in the control group did not have any eye diseases or previous intraocular surgeries. They also had normal anterior segment and fundus vision, a best corrected visual acuity (BCVA) of 1.00 or above, intraocular pressure (IOP) within the usual range, and a spherical equivalent within ±6.0 D.

The recruited participants were briefed on the study's nature and goal after the institute's ethical committee gave its approval and the subjects gave their informed consent.

Here is what all patients went through:

Checking intraocular pressure, visual acuity, slit-lamp examination, fundus examination, complete medical history, and standard laboratory tests.

OCT imaging:

Spectralis, made by Heidelberg Engineering of Heidelberg, Germany, is a spectral domain OCT device that was used to acquire all of the OCT images. The eyes were scanned utilizing the Spectralis platform's eye-tracking-based follow-up feature during the follow-up period. By utilizing enhanced-depth imaging OCT (EDI-OCT), the SFCT was assessed. The GCC thickness was determined automatically by the OCT instrument and is defined as the distance between the inner limiting membrane and the outer boundary of the inner plexiform layer. By calculating the distance between the inner limiting membrane and the interface of the retinal pigment epithelium-choriocapillaris using the radial lines through the foveal area, the central retinal thickness (CRT) was automatically determined. To control for fluctuations during the day, all measurements were taken between 9 am and 12 pm.

A total of 61 individual lines of 15 frames, with a 30°×25° volume scan centered at the fovea, were used to create perifoveal volumetric retinal scans utilizing Heidelberg Engineering's automated eye alignment eye-tracking software. The instrument's RNFL protocol (circular 3.5-mm diameter, 768 A-scans) was used to measure the peripapillary RNFL thickness (from the internal limiting membrane to the inner aspect of the retinal pigment epithelium [RPE]) in a standard fashion. The Spectralis software was used for automatic segmentation. The software that came with the Fovea-Disc Alignment system automatically corrected the orientation of the fovea disc. Foveal fixing and segmentation were verified to be accurate in every instance.

An experienced operator at Al-Hussein University Hospital used these techniques to acquire images; after masking themselves to protect their privacy, they evaluated the images for artifacts, alignment, and quality; and last, they conducted macular segmentation. Using the new Spectralis OCT software, this equipment automatically executed layer-by-layer segmentation, which was validated in the B-scans of each imaged eye according to the criteria of Ishikawa et al.,[6].

Statistical Analysis:

For the purpose of data analysis, we utilized the IBM SPSS software package version 20.0. Armonk, New York, is the home of IBM Corp. The qualitative data were described using percentages and numbers. The Kolmogorov-Smirnov test was used to guarantee that the distribution was normal. Quantitative data were represented using the following methods: range (including minimum and maximum), mean, standard deviation, median, and interquartile range (IQR). A 5% level of significance was used to determine the acquired results.

A chi-square test is employed to compare categorical data in different groups. When the quantitative variables are normally distributed, a Student's t-test (t) can be utilized to compare two groups.

3. Results

Table 1. Comparison of demographic data between studied groups (N=60).

VARIABLES	GROUP-A	GROUP-B	TEST	P-VALUE
AGE			1.32	0.21
MEAN±SD	49.88±9.36	48.23±8.49		
RANGE	20-75	29-66		
GENDER			1.47	0.44
MALE	13(43.3%)	12(40%)		
FEMALE	17(56.7%)	18(60%)		

In group-A: The age of participants ranged between 20-75 years with the mean age was 49.88±9.36 years, (table 1; figure 1).

In group-B: The age of participants ranged from 29 to 66 years, with the mean age was 48.23±8.49 years.In group-A: out of 30-patients, 13(56.7%) were males, 17(43.3%) were females. In group-B: out of 30-controls, 12(40%) were males, 18(60%) were females.In this Study we found that age and gender were statistically insignificant.

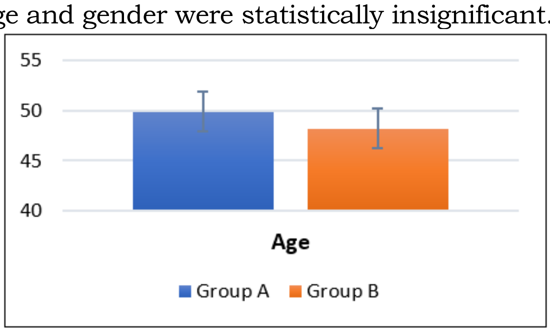

Figure 1. Comparison of age between studied groups.

Table 2. Comparison of HbA1c between studied groups (N=60).

VARIABLES	GROUP-A	GROUP-B	TEST	P-VALUE
HBA1C (%)				
MEAN±SD	7.1±0.5	5.5±0.3	8.35	0.001*
RANGE	6.6-7.8	4.8-5.9		

In group-A: the mean HbA1c value was 7.1±0.5 (range: 6.6–7.8), In group-B: the mean HbA1c value was 5.5±0.3 (range: 4.8–5.9). HbA1c level was significantly higher in the diabetic group compared with the control group. in the diabetic group (P<0.001), (table 2; figure 2).

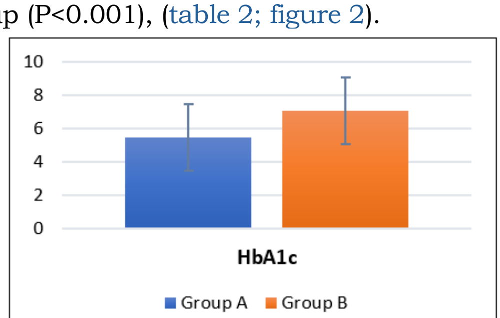

Figure 2. Comparison of HbA1c between studied groups.

Table 3. Comparison of BCVA and IOP between studied groups (N=60).

VARIABLES	GROUP-A	GROUP-B	TEST	P-VALUE
BCVA (LOGMAR)			1.25	0.87
MEAN±SD	0.26±0.29,	0.21±0.15		
RANGE	0-1	0-0.5		
IOP (MMHG)			1.65	0.98
MEAN±SD	15.44±3.1	14.22±2.91		
RANGE	11-21	10-20		

In group-A: the BCVA in LogMAR ranged between 0-1.0 with a mean of 0.26±0.29, In group-B: the BCVA in LogMAR it ranged between 0-0.5 with a mean of 0.21±0.15 which was statistically insignificant (P=0.87), (table 3).

In group-A: the IOP ranged between 11-21 mmHg with a mean of 15.44±3.1 mmHg, in group-B: the IOP ranged between 10-20 mmHg with a mean of 14.22±2.91 mmHg which was statistically insignificant (P=0.98).

Table 4. Comparison of ganglion-cell complex thickness between studied groups (N=60).

GCL–IPL	GROUP-A µM	GROUP-B µM	TEST	P-VALUE
SUPERIOR			8.47	0.002*
MEAN±SD	74.2±15.2	85.11±4.6		
SUPERIOR NASAL			6.18	0.002*
MEAN±SD	79.23±16.33	85.63±3.77		
SUPERIOR TEMPORAL			7.36	0.001*
MEAN±SD	76.21±14.98	82.33±3.11		
INFERIOR			5.14	0.001*
MEAN±SD	68.12±18.99	84.23±16.2		
INFERIOR NASAL			6.49	0.001*
MEAN±SD	72.43±16.98	84.32±10.36		
INFERIOR TEMPORAL			7.63	0.001*
MEAN±SD	75.62±14.39	84.39±2.89		

As regarding GCL–IPL difference, there is a statically significant difference between group-A and group-B in all quadrants as bellow:

Superior: group-A was 74.2±15.2 µm and group-B was 85.11±4.6 µm, Superior nasal: group-A was 79.23±16.33 µm and group-B was 85.63±3.77µm, Superior temporal: group A was 76.21±14.98 µm and group-B was 82.33±3.11µm, Inferior: group-A was 68.12±18.99 µm and group-B was 84.23±16.2 µm, Inferior nasal: group-A was 72.43±16.98 µm and group-B was 84.32±10.36 µm, Inferior temporal: group-A was 75.62±14.39µm and group-B was 84.39±2.89 µm, (table 4; figure 3).

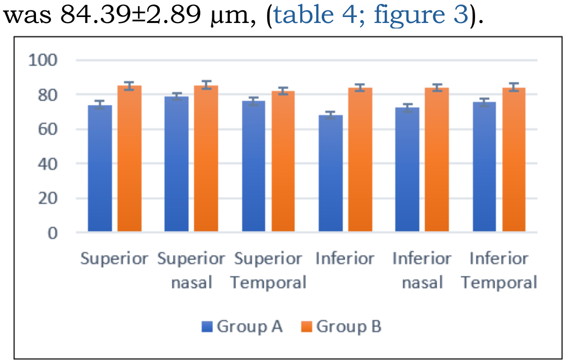

Figure 3. Comparison of GCL–IPL between studied groups.

Table 5. Comparison of Retinal nerve fiber layer between studied groups (N=60).

RNFL	GROUP-A	GROUP-B	TEST	P-VALUE
AVERAGE			6.58	0.001*
MEAN±SD	86.72±13.98	102.9±7.96		
SUPERIOR			5.62	0.001*
MEAN±SD	105.21±19.67	129.65±10.34		
INFERIOR			7.95	0.001*
MEAN±SD	112.67±19.42	128.41±15.54		
NASAL			8.12	0.001*
MEAN±SD	67.32±14.22	79.42±9.12		
TEMPORAL			7.99	0.001*
MEAN±SD	60.87±10.22	68.32±7.14		

A statistically significant (p=0.001) difference between group-A and group-B as regarding RNFL thickness as bellow:

The average: group-A was 86.72±13.98 µm and group-B was 102.9±7.96 µm, Superior RNFL: group-A was 105.21±19.67µm and group-B was 129.65±10.34µm, Inferior RNFL: group-A was 112.67±19.42µm and group-B was 128.41±15.54µm, Nasal RNFL: group-A was 67.32±14.22 µm and group-B was 79.42±9.12µm, Temporal RNFL: group-A was 60.87±10.22µm and group-B was 68.32±7.14µm, (table 5; figure 4).

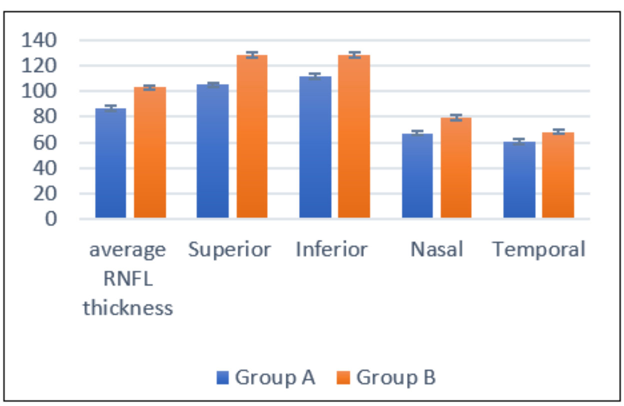

Figure 4. Comparison of average RNFL thickness between studied groups.

Case presentation:

Female patient 46 years old from group-A with type 2 DM for 5 years her HbA1c was 6.9, her right eye BCVA was 0.3 LogMar and IOP was 17 mmHg. Her: CMT=251 µm, GCL+IPL (average)=86 µm, and RNFL (average)=95 µm

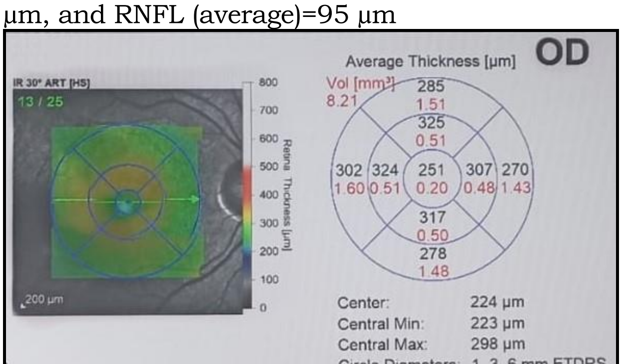

Figure 5. CMT of the right eye of a sample diabetic patient.

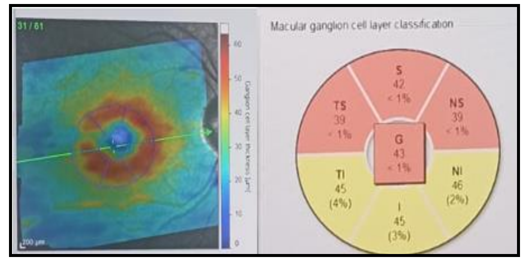

Figure 6.GCL thickness of the right eye of a sample diabetic patient.

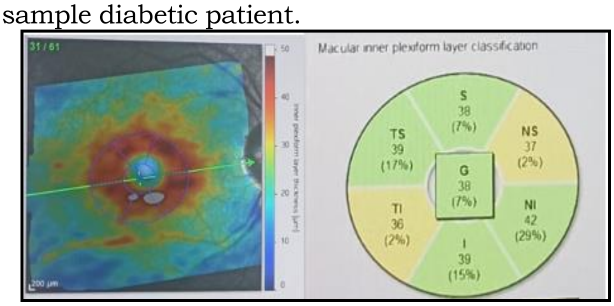

Figure. 7. IPL thickness of the right eye of a sample diabetic patient.

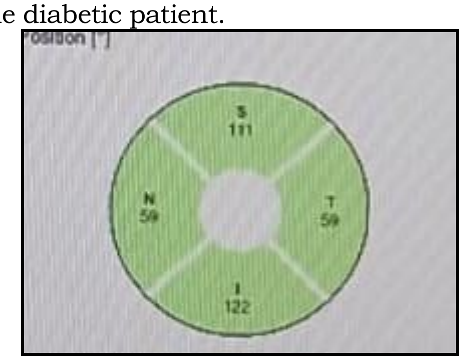

Figure 8. RNFL thickness of the right eye of a sample diabetic patient.

4. Discussion

Among working-age adults, diabetic retinopathy is the most common cause of blindness. About 190 million individuals across the globe are living with DR. A total of 34.6% of persons diagnosed with diabetes mellitus also have DR. DR is a complex disease with multiple risk factors, some of which include serum cholesterol levels, blood pressure, and hemoglobin A1c.[7]

The classic view of DR has focused on it as a microvascular disease with retinal microaneurysms, capillary changes, and hemorrhages as its primary symptoms. As the disease advances, these changes in blood vessel function may cause the inner retina's neuronal and glial components to degenerate. Newer research, however, points to retinal neurodegeneration as occurring before any outwardly apparent microvascular alterations.[8]

Whether diabetic retinal neuropathy is mostly caused by direct neuronal damage from chronic hyperglycemia or by vascular disorders is an ongoing dispute. Functional problems like loss of color discrimination, contrast sensitivity, and dark adaptation are produced by neurodegeneration in DM, which appears to be a systemic process that happens across the macula.[9]

Initiating and activating many metabolic pathways contributes to microangiopathy and the development of DR by breaking the blood-retinal barrier.[10]

Spectral domain optical coherence tomography shows the greatest rate of cell death in retinal ganglion cells, which are also the first cells to be damaged. Axons, nuclei, and dendrites of retinal ganglion cells make up the inner plexiform layer, the layer that contains the nerve fibers of the retina, and the layer that contains the ganglion cells. It is crucial to maintain the integrity of these cells in order to maintain visual function.[11]

Therefore, SD OCT with high resolution can assess the thickness of each individual retinal layer, including RNFL and GCL+IPL, suggesting that ganglion cell loss is the primary cause of their thinning.[12]

As a tool for quantitative investigation of the retina's architecture, optical coherence tomography (OCT) scans the retina's structure in great detail, including its thickness, choroid, and optic disc morphometry. In vivo, optical coherence tomography (OCT) pictures can be utilized for both qualitative and quantitative assessment of retinal disease changes. The diameter of retinal veins and arteries has recently been measured using Spectral Domain OCT. OCT has emerged as a crucial technique for diabetic retinopathy screening, diagnosis, and treatment evaluation Lee et al. [13]

The results showed that in group A, the central foveal thickness varied from 165 to 280 µm, with an average of 233.96±18.63 µm, and in group B, it varied from 240 to 280 µm, with an average of 261.28±11.1 µm (P<0.001).

Ibrahim et al.,[14] also discovered that, when comparing diabetic patients to healthy controls, central foveal thickness was significantly lower in the former group.

We demonstrated in this study that there is a statistically significant relationship between the length of diabetes, hemoglobin A1c, average RNFL thickness, and average GCL-IPL thickness in individuals with diabetes.

Ibrahim et al.,[14] demonstrated a statistically significant relationship between the thickness of RNFL and GCL-IPL and the duration of diabetes and the HbA1c value.

Sugimoto et al.,[15] discovered that RNFL is impacted by glycemic control, namely HbA1c levels, within a four-month timeframe.

Sahin et al.,[16] determined that average RNFL thickness is somewhat inversely correlated with HbA1c, and that RNFL thinning may be associated with higher incidences of atherosclerosis in type 2 diabetic individuals.

Hegazy et al.,[17] discovered a strong inverse relationship between GCL thickness and the duration of DM.

In the results of Toprak et al.,[18] Patients with an HbA1c level of 7% or higher had a noticeably reduced mean RNFL thickness.

Verma et al.,[19] In 2012, researchers observed that individuals with type 2 diabetes who did not have retinopathy and whose hemoglobin A1c levels were less than 7% had significantly reduced mean retinal sensitivity compared to those whose hemoglobin A1c levels were greater than or equal to 7%.

Oshitari et al.,[20] discovered a correlation between HbAc1 and duration, as well as an escalation in the severity of disease, and a correlation between GCs loss and axonal damage.

However, Srinivasan et al.,[21] found no correlation between retinal tissue thickness and HbA1c or diabetes duration.

Improving visual outcome requires early disease detection and prompt treatment. It would be possible to personalize clinical follow-up and therapeutic action if we could identify indicators that reliably predict the likelihood of disease severity and visual outcome.

The lack of inclusion of patients with DR is one of the study's weaknesses.

4. Conclusion

Patients with diabetes who do not have retinopathy had much thinner GCL-IPL and RNFL layers than the control group, suggesting that neurodegenerative alterations brought on by DM occur before vascular abnormalities associated with diabetic retinopathy manifest.

Disclosure

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Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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