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Assessment of Retinal Nerve Fiber Layer Thickness using Optical Coherence Tomograghy (OCT) in patients with Diabetic Retinopathy in relation to HbA1c

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ABSTRACT

Background: Retinal nerve fiber layer (RNFL) thickness loss may contribute to diabetic optic nerve dysfunction if it is not detected early enough.

Aim of The Work: To evaluate the relation of retinal nerve fiber layer thickness to HbA1c in patients with diabetic retinopathy.

Patients and Methods: There were 60 eyes with a Diabetic Retinopathy clinical diagnosis in this cross-sectional trial. Two groups of patients were formed: 30 eyes with diabetic retinopathy in Group A (HbA1c 7%) were included in this study. In the second group B, there were 30 eyes of diabetic retinopathy with uncontrolled glycosylated haemoglobin (HbA1c >7%).

Results: As regard relation between DM duration and eye outcome; it showed highly statistically significant differences between groups according to Auto refractometer (P<0.001), there was no significant association with other eye outcome parameters. As regard correlation between HbA1C and eye outcome and it show highly statistically negative correlation between HbA1C and each of un-corrected visual acuity and best corrected visual acuity.

Conclusion: Even before retinal vascular abnormalities and vision impairment were observed in the majority of the individuals investigated, diabetes had a significant impact on neuronal retinal layer structure. There was a statistically significant link between RNFL quadrant thinning and HbA1c levels above 7% and uncontrolled glucose levels.

Keywords: *Retinal nerve fiber layer thickness; Optic nerve dysfunction; Diabetic Neuropathy.*

INTRODUCTION

In affluent countries, diabetic retinopathy is the most common form of the disease and a leading cause of blindness. Excessive blood glucose levels are one of the most critical causes in the development of diabetes-related retinopathy. Directly affecting retinal cells via hyperglycemia is also critical.[1]

The prevalence of diabetic retinopathy in persons who have had diabetes for a decade or longer is as high as 80%.[2]

One of the numerous aspects that contribute to good eyesight is the ability of the retinal neurons to function normally. Early in diabetes, the quality of vision begins to deteriorate, which may reflect the early stages of neural malfunction.[3]

In the early phases of diabetic retinopathy, the retinal nerve fibre layer is one of the most important structural neurons in the retina. People with diabetes have been found to have RNFL thinning or abnormalities, according to a number of studies. There have been reports of retinal nerve fibre layer loss among diabetic patients without diabetic retinopathy who had a poor glucose control. Another ocular manifestation of diabetes besides diabetic retinopathy could be a malfunction in the retinal nerve fibre layer. RNFL loss may contribute to diabetic optic nerve dysfunction if it is not detected early enough.[4]

OCT is an imaging technique that can be used to diagnose a wide range of eye disorders. RNFL and optic nerve head thickness can be measured objectively and quantitatively with high precision. Diabetic eyes with or without indications of DR show a clinical decrease in the thickness of the central retinal or one cellular layer compared to control groups, according to several studies (persons without DM). In diabetics with mild diabetic retinopathy (DR), the retinal nerve fibre layer in the periphery of the macula thins first, leading to a reduction in inner retinal thickness in the macular area.[5]

Diabetic retinopathy may benefit from the automatic stacking of retinal structures by SD-OCT, according to the findings of Vujosevic and Midena. To prevent and treat diabetes-related vision loss, early detection of retinal nerve fibre layer (RNFL) thinning can benefit ophthalmologists.[6]

In the diagnosis of diabetic individuals at risk for developing problems such as retinopathy, HbA1c is regarded one of the most discriminative and useful techniques. HbA1c and mortality risk variables have recently been linked in men and women with type 2 diabetes. Diabetes patients, particularly those with retinopathy, have higher rates of Gram-positive bacteria, such as Staphylococci, than the general population.[7]

The Aim of the present study was to evaluate the relation of retinal nerve fiber layer thickness to HbA1c in patients with diabetic retinopathy.

PATIENTS AND METHODS

Between the months of February 2021 and January 2022, we examined the retinas of 60 people who had been diagnosed with Diabetic Retinopathy and were seen in the outpatient clinic of the Ophthalmology Department at Al-Azhar University Hospital (Cairo).

Two groups of patients were formed: 30 eyes with diabetic retinopathy in Group A (HbA1c 7%) were included in this study. In the second group B, there were 30 eyes of diabetic retinopathy with uncontrolled glycosylated hemoglobin (HbA1c >7%).

Inclusion criteria: Type I and type II diabetic retinopathy patients (DR).

Exclusion criteria: Presence of any other metabolic disease than DM, opaque cornea, opaque lens, laser retinopexy, intra vitreal injection and intra ocular surgery that have been done within 3 months before OCTassessment, and glaucoma.

Before involvement in the study, all participants were required to sign a consent form.

Everyone was subjected to:

All of medical history.
On the day of the OCT evaluation, a blood sample was collected to determine the HbA1c level.
Attention to detail when performing an OCT exam.

As part of an eye checkup:

Visual acuity, both uncorrected an best corrected.

Applanation tonometer to measure intraocular pressure.

For examination of the anterior section, slit-lamp biomicroscopy is employed.

Slit-lamp biomicroscopy with a 90D lens for dilated fundus examination.

Retinal Nerve Fiber Layer OCT Cross Section (Topcon-DRI OCT Triton-).

Optical Coherence Tomography (OCT):

The thickness of the RNFL was measured using Deep Range Imaging-OCT.(DRI-OCT-1, Topcon, Tokyo, Japan).

A wavelength-swapping laser with an operational range of about 100 nm was used in the Deep Range Imaging-OCT system's creation. More than a million A-scans per second are acquired in tissue with an 8-nm axial resolution. Wide-angle and 3D horizontal (H) disc circle grid scanning of the Deep Range Imaging-OCT were employed in this experiment to examine each eye. Using a quicker scan setting and focusing on the posterior pole, the Deep Range Imaging-OCT image with a 12 9 mm wide-angle was acquired. Ophthalmologic and macular pictures were obtained during one scan.

Optical Coherence Tomography (OCT):

For all of the OCT measurements, there was a single point of contact. The same optical coherence tomography (OCT) apparatus (Topcon DRI OCT Triton + Swept Source OCT version 10.11) was used to evaluate the thickness of retinal nerve fibres in both the anterior and posterior segments (super luminescent LEDs with a wavelength of 1,050nm). In addition, an A-scan rate of 100,000 scans per second is feasible.

The Bab El-Shearyah University Hospital Lab used COBAS INTEGRA 400 plus to evaluate the HbA1c level, and the blood sample was taken the same day as the OCT examination.

Statistical Analysis:

In order to analyze the data acquired, Statistical Package of Social Services version 20 was used to execute it on a computer (SPSS). In order to convey the findings, tables and graphs were employed. The quantitative data was presented in the form of the mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t test (T) is used to assess the data while dealing with quantitative independent variables. Pearson Chi-Square and Chi-Square for Linear Trend (X2) were used to assess qualitatively independent data. The significance of a P value of 0.05 or less was determined.

RESULTS

	Study Group (n = 18)	Control Group (n = 16)	Test of Sig.	P Value
Duration				
Min.-Max.	5-25	5-20	t=2.400	0.022*
Mean± S.D	14.72±6.443	10.19±4.183		
Type				
I	1(5.6%)	0(0%)	X^2=0.916	1.000
II	17(94.4%)	16(100%)		
Treatment type				
Oral	6(33.3%)	10(62.5%)	X^2=2.892	0.168
Insulin	12(66.7%)	6(37.5%)		
HbA1C				
Min.-Max.	7.5-11.30	6.10-6.90	U=0.000	<0.001*
Mean± S.D	9.59±1.153	6.61±0.226		

X2: Chi-square test t: T-student test U: Mann- Whitney test
p: p value for comparing between the two studied groups *: Statistically significant at P <0.05

Table 1: Comparison between two groups as regard to patient's DM characteristics

In Table (1): statistically significant differences between groups based on DM duration (P=0.022) and HbA1C (P<0.001) exhibit DM features.

	Study Group (n = 30)	Control Group (n = 30)	Test of Sig.	P Value
Intra Ocular Pressure (IOP) (mmHg)				
Min.-Max.	12-18	13-19	U=407.50	0.525
Mean± S.D	15.28±1.904	15.13±2.029		
Auto refractometer				
Min.-Max.	-40-3.5	-4.25-6.50	U=338.00	0.097
Mean± S.D	-2.33±9.743	1.30±2.870		
Un Corrected Visual Acurity (UCVA)				
Min.-Max.	0.05-0.33	0.05-0.67	U=312.50	0.039*
Mean± S.D	0.13±0.084	0.22±0.190		
Best Corrected Visual Acurity (BCVA)				
Min.-Max.	0.10-0.50	0.17-1.00	U=273.50	0.007*
Mean± S.D	0.33±0.119	0.45±0.226		
Optical Coherence Tomography (OCT)				
RNFL not Affected	11(36.7%)	30(100%)	X^2=27.805	<0.001*
Affected RNFL Thickness	19(63.3%)	0(0%)		

X2: Chi-square test U: Mann- Whitney test
p: p value for comparing between the two studied groups *: Statistically significant at P <0.05

Table 2: Comparison between two groups as regard to patient's eye outcome

Table (2) demonstrate eye outcome and it show highly statistically significant differences between groups according to Un Corrected Visual Acurity (UCVA) (P=0.039), Best Corrected Visual Acurity (BCVA) (P=0.007) and Optical Coherence Tomography (OCT) (P<0.001).

	DM duration		Test of Sig.	P Value
	<10 years (n = 12)	**>10 years (n = 18)**		
Intra Ocular Pressure (IOP) (mmHg)				
Min.-Max.	13-19	12-18	U=67.00	0.087
Mean± S.D	16.50±1.784	15.17±2.036		
Auto refractometer				
Min.-Max.	-40 – 2	-3.00-3.50	U=24.00	<0.001*
Mean± S.D	-5.33±11.108	1.24±1.746		
Un Corrected Visual Acurity (UCVA)				
Min.-Max.	0.05-0.25	0.05-0.33	U=85.50	0.346
Mean± S.D	0.11±0.063	0.13±0.081		
Best Corrected Visual Acurity (BCVA)				
Min.-Max.	0.10-0.50	0.17-0.50	U=82.50	0.285
Mean± S.D	0.36±0.126	0.31±0.101		
Optical Coherence Tomography (OCT)				
RNFL not Affected	5(41.7%)	6(33.3%)	X^2=0.215	0.712
Affected RNFL Thickness	7(58.3%)	12(66.7%)		

X2: Chi-square test U: Mann- Whitney test
p: p value for comparing between the two studied groups *: Statistically significant at P <0.05

Table 3: Relation between DM duration and eye outcome

Table(3) demonstrate Relation between DM duration and eye outcome and it show highly statistically significant differences between groups according to Auto refractometer (P<0.001).

	DM Treatment type		Test of Sig.	P Value
	Oral (n = 10)	**Insulin (n = 20)**		
Intra Ocular Pressure (IOP) (mmHg)				
Min.-Max.	12-19	12-18	U=96.00	0.880
Mean± S.D	15.60±2.271	15.75±1.943		
Auto refractometer				
Min.-Max.	-40 – 3.5	-4.25-3.00	U=79.00	0.373
Mean± S.D	-4.63±12.805	0.23±2.141		
Un Corrected Visual Acurity (UCVA)				
Min.-Max.	0.05-0.25	0.05-0.33	U=93.00	0.779
Mean± S.D	0.12±0.066	0.13±0.079		

Best Corrected Visual Acurity (BCVA)				
Min.-Max.	0.10-0.50	0.17-0.50	U=83.50	0.475
Mean± S.D	0.35±0.148	0.32±0.091		
Optical Coherence Tomography (OCT)				
RNFL not Affected	5(50.0%)	6(30.0%)	X^2=1.148	0.425
Affected RNFL Thickness	5(50.0%)	14(70.0%)		

X2: Chi-square test U: Mann- Whitney test.
p: p value for comparing between the two studied groups. *: Statistically significant at P <0.05

Table 4: Relation between DM Treatment type and eye outcome

Table(4) demonstrate relation between DM Treatment type and eye outcome and it show no statistically significant differences between groups.

	HbA1C	
	r	**P**
Intra Ocular Pressure (IOP) (mmHg)	0.031	0.812
Auto refractometer	-0.088	0.505
Un Corrected Visual Acurity (UCVA)	-0.319	0.013*
Best Corrected Visual Acurity (BCVA)	-0.450	<0.001*

Table 5: Correlation between HbA1C and eye outcome

Table (5) demonstrate correlation between HbA1C and eye outcome and it show highly statistically negative correlation between HbA1C and each of un-corrected visual acurity (UCVA) (r=-0.319, P=0.013) and best corrected visual acurity (BCVA) (r=-0.450, P<0.001).

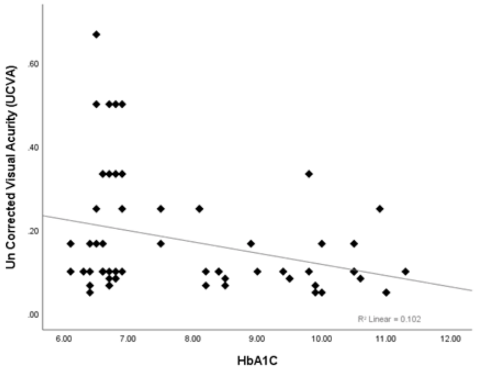

Fig. 1: Correlation between HbA1C and un-corrected visual acurity (UCVA).

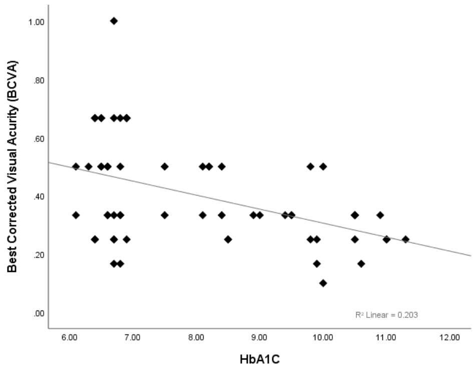

Fig. 2: Correlation between HbA1C and best corrected visual acurity (BCVA)

CASES

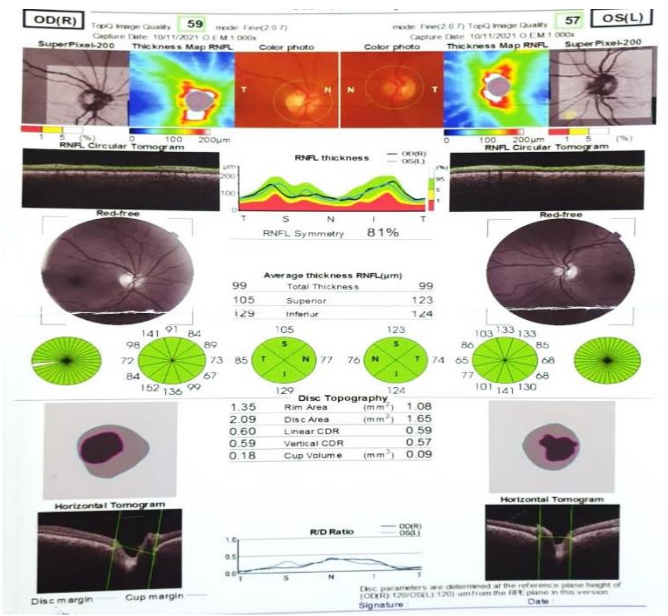

Fig. 3: RNFL not affected.

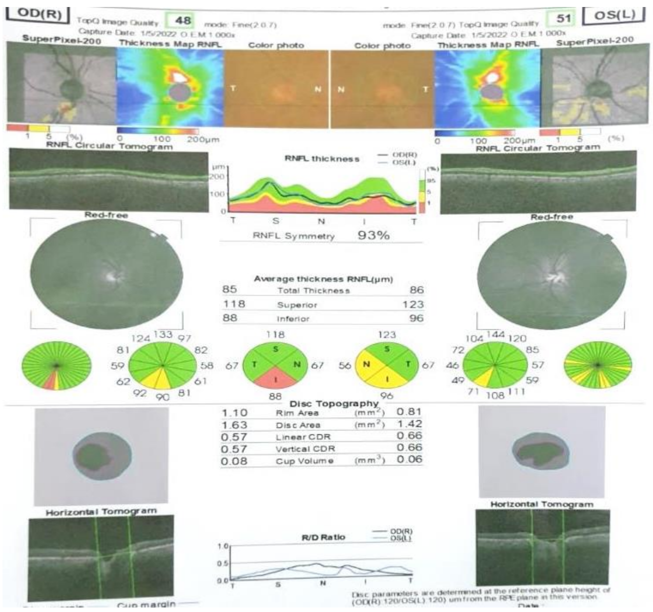

Fig.4: RNFL affected.

DISCUSSION

On the basis of demographic information, there were no discernible disparities between the several groups studied.

Our results coincides with results of Mikhail et al.[8] study, as Uncontrolled diabetics (group 1) had a HbA1c greater than or equal to 7 percent, whereas those who were under control (group 2) had a HbA1c less than 7 percent. There were 16 men (53.3%) and 14 women (46.7%) in the group. Patients in groups 1 and 2 had an average age of 53.53 years and 9.16 years, respectively. Age and sex were not statistically different across the groups (P=0.712 and 0.143, respectively).

The results of this study demonstrate statistically significant differences between groups based on the duration of DM (P=0.022) and HbA1C (P=0.001).

In accordance with our results study of Dhasmana et al.[9] as They found statistically significant differences in the duration of DM and HbA1C levels across their study groups.

While in the study of Borooah et al.[5], Patients with diabetes lived an average of 4.78 ±2.22 years (without DR: 4.21 ±3.03 years; mild DR: 5.35± 3.32), according to the findings of the study. Diabetes patients' HbA1c values were 7.950 ±94% on average (no DR group, 7.721 ±20%, and mild DR, 8.171±20%), according to the study.).

In the study of Lee et al.[10], The DM group had a DM duration of 9.786.48 and a HbA1C score of 7.000. ±0.97.

In the study in our hands, as regard eye outcome and it show highly statistically significant differences between groups according to Un Corrected Visual Acuity (UCVA) (P=0.039), Best Corrected Visual Acuity (BCVA) (P=0.007) and Optical Coherence Tomography (OCT) (P<0.001).

Our results were supported by study of Mikhail et al.[8] as the RNFL thickness in the right eye was statistically significantly lower in the group 1 (P=0.011 and 0.019, respectively) than in the group 2 The inferior RNFL quadrant thickness in the right and left eyes was likewise found to be lower in group 2 (P=0.005 and 0.029, respectively) compared to group 1. As for RNFL metrics, however, there was no statistically significant difference among participants in either group.

Similarly, Borooah et al.[5] revealed that Diabetic patients' RNFLs had an average thickness of 86.18±8.44mm, while controls' measured 91.79±4.77mm (p=0.002). Both groups of diabetes patients had RNFL thicknesses of 86.74% and 85.62%, respectively, in the no-DR group (p=0.697) and in the mild-DR group (p=0.697). Statistics showed statistically significant variations in average thickness of the RNFL between the groups with and without DDR (p=0.027 and p=0.007, respectively) when compared to the controls. The thickness of RNFL in the superior, inferior, and temporal quadrants of diabetic patients and controls varied significantly as well.

Moreover, Chatziralli et al.[11], showed that the IOP in patients with DM and in controls was 14.9 ± 2.3 mmHg and 15.3 ± 3.5 mmHg respectively and did not differ between the two groups ($p = 0.169$). Regarding the peripapillary RNFL thickness, there was a statistically significant difference between patients with DM and controls in average RNFL thickness ($p < 0.001$), as well as in RNFL thickness at superior ($p < 0.001$), inferior ($p < 0.001$), nasal ($p = 0.012$), temporal ($p < 0.001$), inferonasal ($p = 0.018$), inferotemporal ($p < 0.001$), superonasal ($p = 0.005$), and superotemporal ($p < 0.001$) quadrant.

The present study showed that as regard relation between DM duration and eye outcome; it showed highly statistically significant differences between groups according to Auto refractometer (P<0.001), there was no significant association with other eye outcome parameters.

Our results were in line with study of Khalil et al.[12] When Pearson's r test was performed and the duration of DM had a statistically negligible negative association with all of the RNFL thickness measures.

Also, Borooah et al.[5] demonstrated that Patients with diabetes had a non-significant association between their diabetes duration, RNFL thickness, and GCL-IPL thickness.

When it comes to the relationship between DM treatment type and eye outcome, this study found no statistically significant differences across the groups.

In accordance with our results study of Khalil et al.[12] as they revealed that student's unpaired t-test was done to compare between patients controlled by oral hypoglycemic drugs and those controlled by insulin according to different parameters of RNFL across the two groups, all measures related to RNFL thickness (superior, inferior, nasal, temporal, and total) exhibited no statistically significant difference.

In the study in our hands, as regard correlation between HbA1C and eye outcome and it show highly statistically negative correlation between HbA1C and each of un-corrected visual acurity (UCVA) (r=-0.319, P=0.013) and best corrected visual acurity (BCVA) (r=-0.450, P<0.001).

Our results were supported by study of Mikhail et al.[8] as tIn the first section, they found that the thickness of RFNL and GCC decreased significantly when HbA1c was greater than 9%, which is a novel observation. Group 1 had significantly thinner average and temporal quadrants in the right eye as well as both eyes' inferior quadrants in the second half than did Group 2. RNFL quadrants and HbA1c values in group 1 are strongly correlated, according to additional data.

There was a significant difference between diabetic patients and controls in the thickness of the peripapillary RNFL (pRNFL) and its superior and inferior quadrants, as well as the RNFL's average thickness. These findings support those of Gundogan et al.[13]. In addition, there was a significant (P<0.05) negative relationship between HbA1c levels and RNFL thickness in the average and superior quadrants. According to Dhasmana et al[9], patients with DR had an increase in the thickness of the RNFL in the superotemporal and superonasal regions around the optic disc..

Furthermore, Khalil et al.[12] revealed that Pearson's r test was done and RNFL thickness measures and HbA1C had no statistically significant negative correlation.

In addition, Chatziralli et al.[11] demonstrated that results of the multivariate analysis, which examined factors that may affect average RNFL thickness in the diabetic group. Decreased average RNFL thickness was observed to be linked to greater HbA1c, longer duration of diabetes (p = 0.07), and more severe diabetic complications (p = 0.016).

HbA1c levels were found to have no effect on the thickness of the retinal nerve fibre layer (RNFL) in investigations by Peng et al.[15] and Nor-Sharina et al.[14], who employed scanning laser polarimetry to measure HbA1c levels.

Studying 30 diabetics, 30 diabetics with mild disease, and healthy control subjects, Borooah et al.[5] found that the average thickness of the RNFL was 86.18±8.44 and 91.77-9±4.77 in diabetics and controls, respectively (P=0.002). Diabetes duration and HbA1c levels did not have a significant correlation with RNFL and GCC thickness. According to their findings, the neuroretinal changes occur before the vascular abnormalities of DR.

CONCLUSION

In most of the patients tested, diabetes impacted the neuronal retinal layers early, even before the retinal vascular alterations and visual impairment occurred. Thinning of most RNFL quadrants was statistically linked to uncontrolled hyperglycemia with HbA1c more than 7%.

Conflict of interest : none

REFERENCES

1. Singh PP, Mahadi F, Roy A, Sharma P. Reactive oxygen species, reactive nitrogen species and antioxidants in etiopathogenesis of diabetes mellitus type-2. *Indian J Clin Biochem*. 2009; 24:324–42.
2. Williams R, Airey M, Baxter H, Forrester J, Kennedy T, et al. Epidemiology of diabetic retinopathy and macular oedema. *Eye*. 2010; 18: 963-83.
3. Shi R, Guo Z, Wang F, Li R, Zhao L, et al. Alterations in retinal nerve fiber layer thickness in early stages of diabetic retinopathy and potential risk factors. *Current Eye Research*. 2018; 43(2): 244–53.
4. Choi JA, Ko SH, Park YR, Jee DH, Ko SH, et al. Retinal nerve fiber layer loss is associated with urinary albumin excretion in patients with type 2 diabetes. *Ophthalmology*. 2015; 122(5):976-81.
5. Borooah M, Nane YJ, Ekka J. Evaluation of thickness of retinal nerve fiber layer and ganglion cell layer with inner plexiform layer in patients without diabetic retinopathy and mild diabetic retinopathy in type 2 diabetes mellitus patients using spectral-domain optical coherence tomography. *Int J Res Med Sci*. 2018; 6(7): 2434-39.
6. Vujosevic S, Midena E. Retinal layers changes in human preclinical and early clinical diabetic retinopathy support early retinal neuronal and Muller cells alterations. *J Diabetes Res*. 2013; 13: 905-8.
7. Lutty GA. Effects of diabetes on the eye. *Invest Ophthalmol Vis Sci*. 2013; 54(14): 81–7.
8. Mikhail ME, Saif MYS, Mohammad SI. Correlation of retinal nerve fiber layer and ganglion cell complex thickness with glycosylated hemoglobin in diabetic patients. *Delta Journal of Ophthalmology*. 2021; 22(1): 34-8.
9. Dhasmana R, Sah S, Gupta N. Study of Retinal Nerve Fibre Layer Thickness in Patients with

Diabetes Mellitus Using Fourier Domain Optical Coherence Tomography. *Journal of Clinical and Diagnostic Research.* 2016; 10(7): 5–9.

10. Lee MW, Lim HB, Kim MS, Park GS, Nam KY, et al. Effects of prolonged type 2 diabetes on changes in peripapillary retinal nerve fiber layer thickness in diabetic eyes without clinical diabetic retinopathy. *Scientific Reports*. 2021; 11(1): 1-8.
11. Chatziralli I, Karamaounas A, Dimitriou E, Kazantzis D, Theodossiadis G, et al. Peripapillary retinal nerve fiber layer changes in patients with diabetes mellitus: a case-control study. *Seminars in Ophthalmology*. 2020; 35: 257-60.
12. Khalil HF, Ali AEM, Ibrahim MMA, Hatata AFM. Assessment of retinal nerve fiber layer thickness using optical coherence tomography in patients with type 2 diabetes mellitus. *The Egyptian Journal of Hospital Medicine*. 2019; 76(7): 4452-8.
13. Gundogan FC, Akay F, Uzun S, Yolcu U, Cagiltay E, et al. Early neurodegeneration of the inner retinal layers in type 1 diabetes mellitus. *Ophthalmologica*. 2016; 235:125–32.
14. Nor-Sharina Y, Zunaina E, Shatriah I, Win-Mar K, Azriani A. Correlation of retinal nerve fibre layer thickness with HbA1c and oxidised LDL in non-proliferative diabetic retinopathy. *J Diabetes Metab*. 2013; 4:1–6.
15. Peng PH, Lin HS, Lin S. Nerve fibre layer thinning in patients with preclinical retinopathy. *Can J Ophthalmol.* 2009; 44:417–22.