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Assessment of Macular Thickness and Retinal Nerve Fiber Layer Thickness by Spectral Domain OCT in Patients with Type 2 Diabetes Mellitus Without Clinical Diabetic Retinopathy in Relation about the Glycemic Status and Oxidized Low Density Lipoprotein levels

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Abstract

Diabetes retinopathy (DR) is a vascular disorder affecting the microvasculature of the retina. It is estimated that diabetes mellitus affects 4%of the world's population, almost half of whom have some degree of DR at any given time. Diabetes mellitus is the leading cause of new cases of blindness among adults aged 20 to 74 years. India has more the 62 million diabetic subjects at present as per WHO estimates (8). The prevalence of DR in Winconsin epidemiological study of diabetic retinopathy (WESDR) was 99%in Insulin-dependent diabetes mellitus (IDDM) & 60% in noninsulin-dependent diabetes mellitus (NIDDM) Prevalence of DR was 54.2% in the Diabetes Control and Complication Trial (DCCT) study in IDDM and 35-39% in the United Kingdom Prospective Diabetes Study in NIIDM (5). In the Andhra Pradesh Eye Disease Study (APEDS) of self-reported diabetics the prevalence of DR was 22.4% in the Chennai Urban Rural Study (CURES), done in 2005 they evaluated the urban sample of diabetic patients and estimated the overall prevalence of DR as 17.6% (9). This study aims to measure retinal nerve fiber layer thickness & macular thickness in diabetic patients without retinopathy, by Spectral Domain Optical Coherence Tomography (SD-OCT) and to find out which quadrant has the maximum change in thickness. The study aims to find the clinical significance of the correlation for practical use.

Keywords: Diabetes retinopathy, WESDR, IDDM, NIIDM, Macular Thickness, RNFL Thickness

Introduction

Diabetes mellitus is the leading cause of new cases of blindness among adults aged 20 to 74 years. Diabetes retinopathy (DR) is a vascular disorder affecting the microvasculature of the retina.

It is estimated that diabetes mellitus affects 4%of the world's population, almost half of whom have some degree of DR at any given time. DR occurs both in type 1 & type 2 Diabetes mellitus and has been shown that nearly all type 1 and 75% of type 2 DM will develop DR after 15 years of duration of diabetes (1,2).

Prevalence of DR in winconsin epidemiological study of diabetic retinopathy (WESDR) was 99%in Insulin dependent diabetes mellitus (IDDM) & 60% in Non Insulin dependent diabetes mellitus (NIDDM) Prevalence of DR was 54.2% in the Diabetes Control and Complication Trial (DCCT) study in IDDM and 35-39% in United Kingdom Prospective Diabetes

study in NIIDM (5). Majority of the patients have NIIDM or type 2 diabetes. In two studies from south India, done in 2004 the prevalence rate of DR in NIIDM patients were 34.1% and 37% (6,7). India has more the 62 million diabetic subjects at present as per WHO estimates (8). In the Andhra Pradesh Eye Disease Study (APEDS) of self reported diabetics the prevalence of DR was 22.4% in the Chennai Urban Rural Study (CURES), done in 2005 they evaluated the urban sample of diabetic patients and estimate the overall prevalence of DR as 17.6% (9).

Particularly vision loss in diabetes mellitus is seen in uncontrolled glycemic levels. Moreover, once set in, requires frequent ophthalmic examination and high-cost drugs (eg. Bevacizumab) for treatment. However it is preventable by achieving the glycemic control and reducing the disease duration.

HbA1c is glycosylated haemoglobin. It is formed due to non-enzymatic glycation pathway by hemoglobins exposure to plasma glucose and reflects the blood glucose over the last 8 to 12 weeks. In diabetes mellitus, higher amount of glycated haemoglobin, indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy and retinopathy. Monitoring HbA1c levels may improve outcome (10).

Oxidised low density lipoprotein (LDL) derived from LDL cholesterol under oxidative stress, encompasses many atherogenic properties. Oxidised LDL is an independent predictor of endothelial dysfunction with pro-inflammatory, pro-thrombotic and pro-apoptotic properties in individuals suffering from oxidized stress such as diabetic patients. Guidelines for the management of the lipid profile in diabetic patients are mainly focused on controlling LDL cholesterol, triglycerides, high density lipoprotein-cholesterol and total cholesterol. To date, there is still a lack of data concerning the role of atherogenic lipids such as oxidised LDL among diabetic patients with retinopathy, whether there is a significant correlation between oxidised LDL with the retinal nerve fiber layer. Higher total and LDL cholesterol levels were each associated with severity of hard exudates. In a prospective analysis of ETDRS data (11), the development of hard exudate was 50% faster among subjects with elevated baseline levels of total cholesterol and triglycerides and 36% faster among participants with higher baseline of LDL compared with participants with normal lipid levels at baseline in small study. In another smaller study of type 1 diabetes, those who had higher cholesterol levels had a 46% higher incidence of macular edema.

Hyperglycemia is also associated with dyslipidemia, specifically increased levels of total cholesterol and triglycerides, a slight elevation of LDL, but generally little if any change in HDL, resulting in increased total-to-HDL cholesterol ratio. Consequently, we think that the potential for confounding demands adjusting for HbAlc to assure that any observed association between lipids and retinopathy is not a spurious finding.

Spectral domain OCT allows for non-invasive in vivo cross-sectional image of ocular structure such as retina, RNFL and optic nerve head. Spectral domain OCT applies the principle of interferometry to determine the interface between different ocular tissue. Using automated segmentation algorithms based on reflectivity changes between adjacent retinal layers, the RNFL thickness can be calculated (12,13,14,15),

"Thus the purpose of study is to evaluate if poorly controlled diabetes -as reflected by high recent HbA1c levels causes thinning of the nerve fibres & to asses if there is a significant correlation between atherogenic lipids (oxidised LDL) with the retinal nerve fiber layerand macular thickness."

Diabetes Mellitus:

The history of diabetes started in approximately 1550 BC. An Egyptioan papyrus mentioned a rare disease that causes the patient to lose weight rapidly and urinate frequently. This is thought to be the first reference of the disease.

Diabetes was given its name by the Greek Physician Aretaeus (30-90 CE). He recorded a disease with symptoms such as constant theist, excessive urinations loss of weight. He named the condition diabetes, meaning ‘a flowing through’.

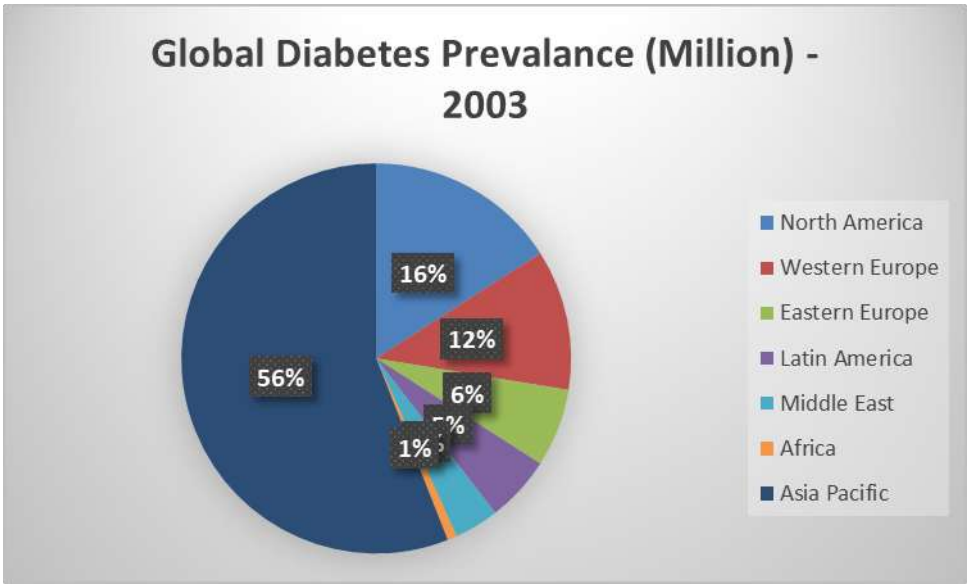
Later, Galen (131-201CE) noted the rarity of this condition and theorized that it was an affliction of the kidneys. He named the disease “Diarrhea of the urine”. After this period, diabetes was rarely mentioned. Indeed, it seemed to have been a mystery or incredibility rare during the Middle Ages. The first clear reference to this disease came from Avicenna.,

Volume 7, Issue 1; January-February 2024; Page No 164-178

the famous Arabian Physician. He described in detail the complication of the disease and how it happened.

Indian Physician Sushruta and Charaka identified Type 1 and Type 2 diabetes as separate condition for the first time in 400-500 AD: type 1 associated with young and type 2 associated with being overweight. The term" mellitus" or "from honey" was added by Briton John Rolle in the late 1700s to separate the condition from diabetes insipidus, which is also associated with frequent urination. Effective treatment was not developed until the early part of the 20th century, when Canadians Frederick Banting and Charles Harbert Best isolated and purified insulin on 1921 and 1922. This was followed by the development of the long-acting insulin NPH in the 1940s. Birth date of Best, 14th November is celebrated as World Diabetes Day.

Globally, as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases (16), In 2013, according to International Diabetes Federation, an estimated 381 million people had diabetes. Its prevalence is increasing rapidly, and by 2030, this number is estimated to almost double (17), Diabetes mellitus occurs throughout the world, but is more common (especially type 2) in the more developed countries. The greatest increase in prevalence is, however, expected to occur in Asia-Pacific, where most patients will probably be found by 2030. The increase in incidence in developing countries follows the trend of urbanization and lifestyle changes, perhaps most importantly a "Western-style" diet.



India has more diabetics than any other country In the world, according to the International Diabetes Foundation,(18) although more recent data suggest that China has even more. According to the Indian Heart Association, India is the diabetes capital of the world with a projected 109 million individuals with diabetes by 2035 (19). The disease, currently affects more than 62 million Indians, which is more than 7.1% of India's adult population. An estimate shows that nearly 1 million Indians die due to Diabetes every year (20). The average age of onset is 42.5 years (20). The high incidence is attributed to a combination of genetic susceptibility plus adaption of a high calories, low-activity lifestyle by India's growing middle class (21). Additionally, a study by the American Diabetes Association reports that India will see the greatest increase in the people diagnosed with diabetes by 2030.

Diabetes Mellitus is ac chronic disease that occur either when the pancreas does not produce enough insulin or the body cannot effectively use the insulin it produces. Insulin is a hormone that regulate blood sugar (22). Hyperglycemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over

Volume 7, Issue 1; January-February 2024; Page No 164-178

time leads to serious damage to many body's system, especially the nerves and blood vessels.

Type 1 diabetes: Type 1 diabetes (previously known as insulin dependent, juvenile or childhood onset) is characterized by deficient insulin production and requires daily administration of insulin. The cause of this type 1 Diabetes in not known and it is not preventable with current knowledge.

Symptoms include excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger, weight loss, vision change and fatigue. These symptoms may occur suddenly.

Type 2 diabetes (formerly called non-insulin-dependent or adult-onset): results from the body's ineffective use of insulin. Type 2 diabetes comprises 90% of people with diabetes around the world (7), and is largely the result of excess body weight and physical inactivity.

Symptoms may be similar to those of Type I diabetes, but are often less marked. As a result, the disease may be diagnosed several years after onset, unce complications have already arisen.

The importance of protecting the body from hyperglycemia cannot be overstated; the direct and indirect effects on the human vascular tree are the major source of morbidity and mortality in both type 1 and type 2 diabetes. Generally, the injurious effects of
hyperglycemia are separated into macrovascular complications (coronary artery disease, peripheral arterial disease, and stroke) and microvascular complications (diabetic nephropathy, neuropathy, and retinopathy).

Criteria for Diagnosis of Diabetes Mellitus- Symptoms of diabetes plus random blood glucose concentration >/= 11.1 mmol/L (200 mg/dL)
• Fasting plasma glucose >/= 7.0 mmol/L (126mg/dL)
• HbA1c > 6.5 or
• Two hour post prandial plasma glucose >/= 11.1 mmol/L during an oral glucose tolerance test

Retinal Nerve Fiber Layer Thickness in Diabetes and its Association with Glycemic Status and Lipid Profile:

Normal vision depends on the normal function of the retinal neurons to produce a good quality of vision. The quality of vision starts to deteriorate early in diabetes, before the clinical retinopathy becomes evident, probably indicating the early signs of neuronal dysfunction.

RNFL is an important structural neuron in the retina layer which is often shown to affect in the early pathogenesis of diabetic retinopathy. Several studies have reported RNFL thinning or defects in people with diabetes. Histological studies of neural components of the retina have revealed that diabetes induced biochemical mechanisms can potentially cause neural cell degeneration, An in-depth understanding of the vascular changes in the retina during diabetes has given cause for the treatment of diabetic retinopathy. Indeed, the only proven treatment for diabetic retinopathy apart from intensive insulin therapy is laser photocoagulation, which involves the destruction of the retinal regions which contains overt vascular abnormalities. Subsequently, early detection of RNFL thinning may help ophthalmologists to provide effective treatment of diabetic retinopathy and with early prevention, thus reducing vision loss.

Nowadays, due to the new introduction of imaging devices such as Heidelberg Retina Tomograph (HRT) and optical coherence tomography (OCT), RNFL thickness can be measured quantitatively and evaluated in vivo.

Besides this, we also noticed that the thickest RNFL in nasal quadrant might be due to the lack of micro aneurysm presence in this area and therefore less retinal nerve fiber layer damage occurred in this quadrant.

Studies concerning RNFL thickness in diabetes are very rare from Asia. One landmark study from Japan found significant RNFL. thinning in diabetics (Oshitari et al., 2009). In that study, they also found significant differences of RNFL thickness according to gender. However, once proliferative changes developed, there was macular thickening (Oshitari et al., 2009). In another prospective study from Korea, the authors found significant peripapillary thickening in retina, correlating with the severity of diabetic retinopathy (Cho et al, 2010). However, our study was with patients in early stage of retinopathy or no overt retinopathy. Further studies

Volume 7, Issue 1; January-February 2024; Page No 164-178

are needed to find the changes in RNFL with time. Extensive literature search could not reveal any Indian study on RNFL thickness in diabetes.

Review Of Literature:

Prevalence of diabetic retinopathy globally:

Studies performed across the globe reported varying rates of prevalence such as Lianet al. (39%) in Hong Kong. Rodriguez-Poncelaset al. (12.3%) in Spain, Dawkins et al. (18.6%) in Timor-Leste, Huang et al. (33,9%) in Singapore, Giloyanet al. (36.2%) in Armenia, Hajaret al. (27.8%) in Saudi Arabia, and Dutra Medeiros et al. (16.3%) in Portugal.

A pooled individual participant meta-analysis involving 35 studies conducted worldwide from 1980 to 2008, estimated global prevalence of any DR and PDR among patients with diabetes to be 35.4 and 7.5 % respectively.

Prevalence of any DR and PDR was higher in those with type I diabetes, compared to those with type 2 diabetes (77.3 vs. 25.2 % for any DR, 32.1 vs. 3.0 % for PDR).

In general, patients with type 2 diabetes in Western communities have a higher prevalence of DR than their Asian counterparts. In the USA, studies estimate that 28.5-40.3 96 or patients with type 2 diabetes had DR, and 4.1-8.2 % of them had VTD Rown in contrast, most Asian countries report DR prevalence to be between 12.1-23.0 %, and VTDR prevalence to be between 4.3-4.6 %.

Incidence of diabetic retinopathy globally:

There are few population-based cohort studies, outside of the USA or UK, which have investigated DR incidence.

In the USA, the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) found that among patients with insulin-dependent diabetes with onset before the age of 30, who are presumed to have type 1 diabetes, the 4-year cumulative incidence of DR was 59.0%. At 10, 14 and 25 years, cumulative incidence of DR in the same cohort rose to 89.3%, 95.9% (9) and 97 % respectively.

The Blue Mountains Eye Study in Australia reported a cumulative 5-year incidence of DR of 22.2% in those diagnosed with diabetes at baseline, while progression to proliferative DR occurred in 4.1% of those who had DR at baseline.

The DR screening program in the UK has reported the 5-ycar cumulative incidence of any DR as 36%, proliferative DR as 0.7% and DME as 0.6%, rising to 66%, 1.5% and 1.2% respectively after 10-years follow-up.

The India Scenario Of Diabetic Retinopathy:

According to statistics from the International Diabetes Federation (IDF), India has more diabetics than any other nation of the world. Current estimates peg the number of diabetics in the country at about 62 million - an increase of over 10 million from 2011 when estimates suggested that about 50.8 million people in the country were suffering from the disease. If you think the disease has already reached endemic proportions in the country, consider this. By the year 2030, over 100 million people in India are likely to suffer from diabetes.

The Chennai Urban Rural Epidemiology Study (CURE):

Eye study is a population- based study conducted on a representative population of Chennai (formerly Madras) city in South India to assess the prevalence of diabetic retinopathy (DR) in type 2 diabetic subjects in urban India using four-field stereo color photography. The overall prevalence of DR in the population was 17.6% (95% Cl:15.8-19.5, which included 20.8% (95% CI:18.7-23.1) in known diabetic subjects and 5.1% (95% Cl: 3.1-8.0) in subjects with newly detected diabetes. The prevalence of DR was significantly higher in men than in women (21.3% vs. 14.6%; P < 0.0001) and among subjects with proteinuria (P = 0.002). Logistic regression analysis showed that for every 5-year increase in the duration of diabetes, the fISk for DR increased 1.89-fold (95% Cl: 1.679-2.135; P < 0.0001). For every 2% elevation of glycated hemoglobin (UbA1c), the risk for DR increased by a factor of 1.7 (95% Cl: 1.545-1.980; P <0.0001).

Prevalence of diabetic retinopathy in India: The All-India Ophthalmological Society Diabetic Retinopathy Eye Screening Study 2011:

A total of 6218 known diabetes were creened. Totally, 5130 data entry forms were considered

Volume 7, Issue 1; January-February 2024; Page No 164-178

suitable for further evaluation. About 61.2% were males, 88.6% were between 40 and 80 years of age, almost two-thirds of the patients were from the west and south zones, and over half had diabetes more than 5 years. The data set was predominantly urban 84.7% and 46.1% had no family history. DR prevalence in the entire data set was 21.7%. Prevalence was more in males (P = 0.007). diabetics more than 5 years (P = 0.001), those above 40 years (P = 0.01), insulin users (P =0.001), and history of vascular accidents (P = 0.0014). Significantly 22.18% of patients detected with DR had a vision of 6/18 or better in the worse eye. The study reiterated the findings of earlier regional studies on a pan Indian scale and put data in perspective.

Material & Methodes:

1. Study area : Department of Ophthalmology, DRISHTIDEEP EYE INSTITUTE
2. Study population: Patients attending Department of Ophthalmology OPD of DRISHTIDEEP EYE INSTITUTE
3. Sample size- 40 patients- Type 2 Diabetic patients without any evidence of diabetic retinopathy. A total of 80 eyes were observed
4. Study design: Cross sectional, hospital-based study

Explanation Of Procedure:

If you agree to participate in this study, we will collect some relevant information fiom your hospital records. We would be doing certain tests like Direct Ophthalmoscopy, Visual Acuity, US B Scan etc. and these tests would not be charged. Data from the study will be used for research purpose only. The results of the study will not be made available to you. All the analysis will be made with an intention to treat. This is to inform you that there are some risks involved in the process of study but the chances of the same are minimal. Serious life threalening reactions are exceptionally.

Potential Benefits:

Your participation will help us in managing this problem in you and other patients and results of this study will also be beneficial for future generations.

Assurance Of Confidentiality:

The information concerning your participation in the study will be kept confidential to the full extent permitted by law and used only for scientific purpose. No one except members of the research team will have access to test results. Your name will not be used in any report or released in any way.

Consent:

A written consent was taken by the patient mentioning the pros and cons of the research work. The patients were given full opportunity to discuss about the study and had full right to quit anytime from the study when desired.

Clinical Examination:

Data collected from the patients' records included patient's age, gender, duration of diabetes mellitus, age at onset of diabetes mellitus, presence or absence of hypertension use of insulin or oral hypoglycemic agents, presence of other systemic diabetic complications and other general illness. All patients undergone biological workup including:

FBS- fasting blood sugar at first contact with patient
PPBS- post prandial blood sugar at Erst contact with the patient
HbA1c & oxidized LDL. levels at the first contact with the patient

All the patients underwent the following tests on the first day of visit and then registered for further evaluation-

1. Visual acuity using Snellen's chart
2. Vision with pin hole* Refraction by autorefractometer and best corrected visual acuity (BCVA)
3. Slit lamp examination & Slit lamp bio-microscopy with +78D or +90D lens.
4. Distant direct ophthalmoscopy
5. Indirect ophthalmoscopy
6. Spectral domain OCT (Cirrus HD-OCT, Carl 'Zeiss Meditec, Dublin, CA)

Inclusion Criteria:

Cases:

Type 2 Diabetic patients of both sexes without retinopathy receiving treatment at OPD clinic of S. S. Hospital BHU, Varanasi.

Only adults (>18years of age)

Volume 7, Issue 1; January-February 2024; Page No 164-178

Exclusion Criteria:

Patients having ophthalmoscopic conditions where evaluation of fundus by +90D or

+78D Jenses, indirect ophthalmoscopy and spectral domain OCT procedures cannot be possible (like nuclear sclerosis grade 3 & onward cataracts, complicated cataracts, cortical cataracts & dense media opacities which hinders the evaluation)

1. Neural ophthalmic conditions
2. High myopia
3. Glaucoma
4. Patients taking retinotoxic drugs like hydrochloroquin
5. Hypertensive patients

All patients were refracted, and BCVA was measured using the Smellen's visual acuity chart. In addition to other routine ophthalmic examinations, spectral-domain

OCT (Cirrus HD-OCT, Carl Zeiss Meditec, Dublin, CA) was performed in all eyes with à6. mim line scan, which comprises 1,024 axial scans, through the central fovea in Oh the horizontal and vertical directions. We also obtained images using the Currently available Cirrus-OCT software (Carl Zeiss Meditec, Dublin, CA) for a macular cube of 512x128, in which a 6x6-mm area of the macula is scanned with 28 horizortal lines, each consisting of 512 A-scans per line. We defined the central subfield thickness (CST) as the average retinal thickness of the I-mm central scanned arca and cystic changes as intra-retinal cystoid spaces in the fovea (1.8 mm in diameter).

Slit Lamp Bi-Microscopy:

Diabetic macular edema can appear as a localized or diffuse macular thickening depending on the severity of retinopathy. The localization of macular edema can be guided by the presence of characteristic elements such as microaneurysms and hard exudates.

Optical Coherence Tomography (Oct):

OCT represents an important tool, helpful both in the diagnosis and follow-up procedure. OCT is an optical technique for high resolution, cross-sectional imaging of tissue. It is analogous to computed tomography, which uses X rays; magnetic resonance, which uses spin resonance and ultrasound B scan, which uses sound waves. OCT uses a super-luminescent diode as its light source. It can perform micron resolution up to <10 microns on cross-sectional or topographical imaging in biological tissues.

Statistical Analysis:

Statistical analysis was performed using software.

Master chart was prepared by Microsoft excel & then loaded onto the SPSS software.

Descriptive statistical analysis was performed to prepare different frequency tables and to calculate the means with corresponding standard errors. Pearson Chi Square test was applied as measure of association. $P<0.05$ was taken to be statistically significant.

Observation Table:

Total number of patients studied is 40

Both eyes of the patient were studied (80 eyes)

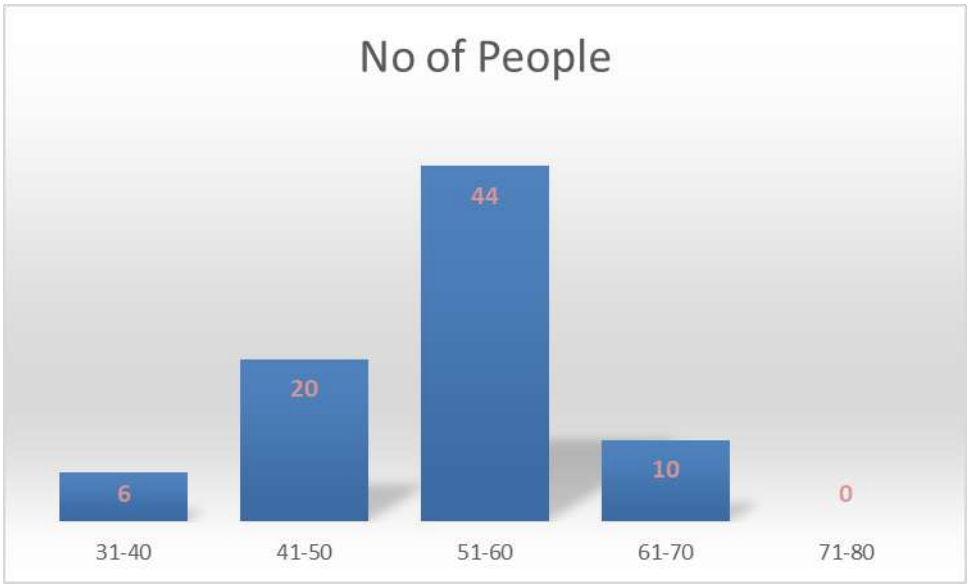
Minimum age of the subject under study is 35

Maximum age of the subject under study is 65

Total number of males is 28

Total number of females is 12

Volume 7, Issue 1; January-February 2024; Page No 164-178



X-axis shows age in years.

Y-axis shows number of subjects.

Total number of subjects: 40

Minimum age of the subject: 35 years

Maximum age of the subject: 65 years

Range - 30 years (35-65)

Mean age of patient: 53.40 years +/-7.28 years.

Table 1: Showing age distribution among the study group

Age in Years	Count	Percentage
31-40	6	7.5
41-50	20	25
51-60	44	55
61-70	10	12.5

Maximum number of patient s belongs to the gr group of 51-60 years (55%)

Volume 7, Issue 1; January-February 2024; Page No 164-178

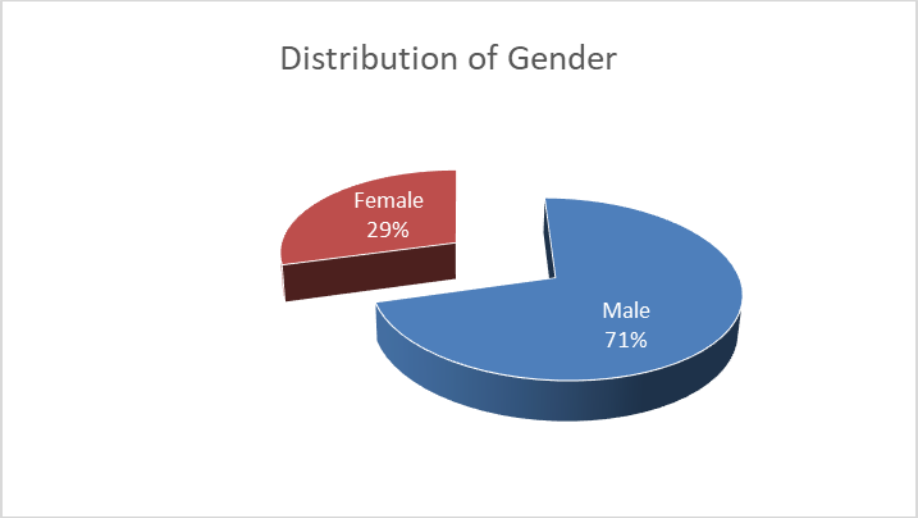


Table 2: Showing gender distribution among the study group

Gender	Count	Percentage
Male	58	70
Female	24	30

Table 3: Showing gender distribution among the various age group

Age in Years	Count	Count of Male	Count of Female
31-40	6	2	4
41-50	20	10	14
51-60	44	36	8
61-70	10	8	2
71-80	0	0	0
Total	80	58	24

Table 4: Statistical correlation between fasting blood sugar (FBS) with Retinal Nerve Fiber Layer thickness in all quadrants

Volume 7, Issue 1; January-February 2024; Page No 164-178

FBS (mg/dl)	Mean+/- SD	f-value	p-value
<100	101.00 +/- 12.336	32.827	<0.001
100-126	124.00+/- 13.543		
>126	135.00+/- 11.015		

p-value is <0.001, hence the result is statistically significant.

Table 5: Statistical correlation between post prandial blood sugar (PPBS) with Retinal Nerve Fiber Layer thickness in all quadrants

PPBS (mg/dl)	Mean+/- SD	f-value	p-value
<140	154.38 +/- 20.827	21.184	<0.001
140-200	187.11+/- 24.523		
>200	199.00+/- 19.900		

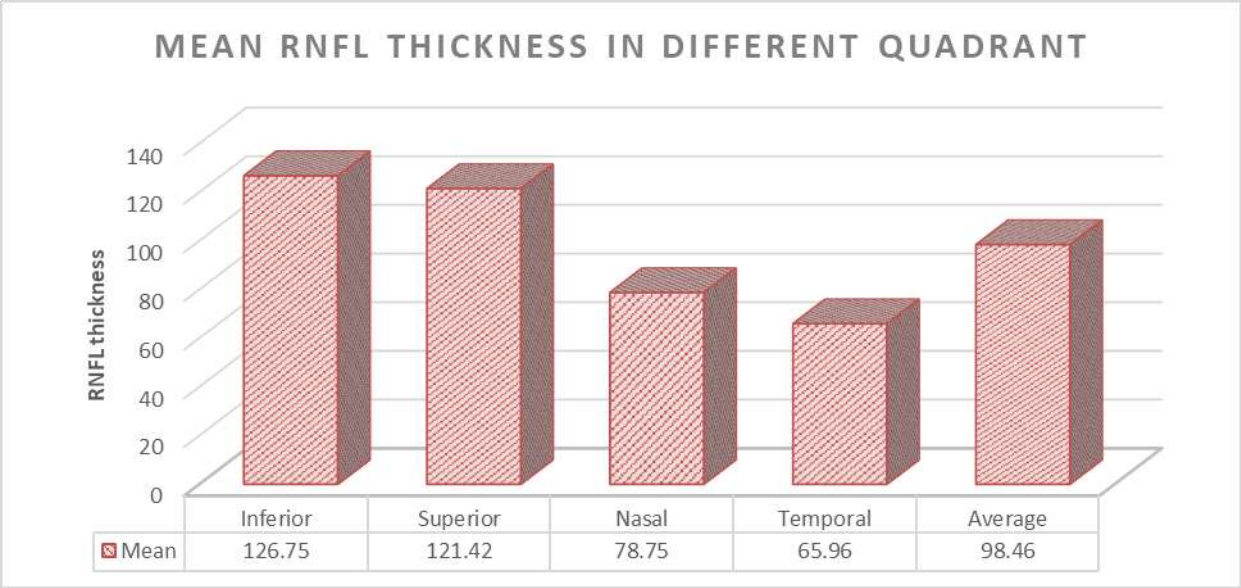
Retinal Nerve Fiber Layer Thickness:

Table 6: Showing the Mean Retinal Nerve Fiber Layer Thickness in all quadrant

Quadrants	Mean	Standard Deviation
Inferior	126.75	14.7863
Superior	121.42	11.7621
Nasal	78.75	18.9890
Temporal	65.96	12.5541
Average	98.46	10.7671

Showing Mean Retinal Nerve Fiber Layer Thickness in all quadrant (in Micro Meter)

Volume 7, Issue 1; January-February 2024; Page No 164-178



Chi Square Test:

Table 7: Statistical correlation between Inferior RNFL thickness with HbA1c

	Value	Df	Asymp.Sig (2-Sided)
Person Chi Square	19.84	4	0.0005
No. of Valid Cases	80		

P value is 0.0005, hence the result is statistically significant.

Table 8: Statistical correlation between Superior RNFL thickness with HbA1c

	Value	Df	Asymp.Sig (2-Sided)
Person Chi Square	32.32	4	<0.001
No. of Valid Cases	80		

P value is <0.001, hence the result is statistically significant.

Table 9: Statistical correlation between Nasal RNFL thickness with HbA1c

	Value	Df	Asymp.Sig (2-Sided)

Volume 7, Issue 1; January-February 2024; Page No 164-178

Person Chi Square	6.79	4	0.146
No. of Valid Cases	80		

P value is 0.146, hence the result is not statistically significant

Table 10: Statistical correlation between Temporal RNFL thickness with HbA1c

	Value	Df	Asymp.Sig (2-Sided)
Person Chi Square	0.629	2	0.7299
No. of Valid Cases	80		

P value is 0.7299, hence the result is not statistically significant

Table 11: Statistical correlation between Average RNFL thickness with HbA1c

	Value	Df	Asymp.Sig (2-Sided)
Person Chi Square	35.14	4	<0.001
No. of Valid Cases	80		

P value is <0.001, hence the result is statistically significant.

Discussion:

Advances in ocular imaging technology have made it possible to evaluate the RNFL thickness in an objective, quantifiable, and reproducible fashion, Optical Coherence Tomography (OCT), which uses short coherence length interferometer, has a fine resolution (up to 2 microns) and reflects the histologic characteristics of the tissue. Because OCT is based on the cross-sectional image of the retina, the instrument measures the nerve fibre layer directly, has no need for a reference plane, and is known to be unaffected by the refractive status, axial length of the subject, sclerosis of the lens, or pupillary dilation. The only limitations of OCT imaging are the uncertainty of the assumed group refractive index of tissue, the effect of eye movements during the B-scan location, and the interface detection artifacts. The Cirrus HD-OCT, Carl Zeiss Meditec, Dublin, CA has eye tracking system and it negate the effect of the eye movements. To avoid any influence of the eye movements, we observed the scanned eye software interface detection artifacts, we inspected every B-scan and repeated the scan if we noticed any eye movements. To avoid software interface detection artifacts, we inspected every B-scan after acquisition and repeated the scan if the software was unable to detect the RNFL borders.

Previous studies have shown that in patients with diabetes mellitus, poor glycemic control leads to

Volume 7, Issue 1; January-February 2024; Page No 164-178

infarction in the nerve fiber layer leading to axonal degeneration and decrease in inferior, decrease in the number of optic nerve axons and the number of retro-bulbar optic nerve fibers (100-103).

Two studies of the retinal nerve fiber layer have shown both broad and slit like defects, suggesting that retinal nerve fiber loss and optic nerve fiber loss are related to subclinical vision loss in diabetic patients without any clinical retinopathy.

The Purpose Of Our Study Was To Measure:

A. Retinal nerve fiber layer (RNFL) thickness in diabetic patient without retinopathy and find out which quadrant has maximal change in thickness in relation to the glycemic levels. During study period 80 eyes of 40 patients with type 2 diabetes mellitus without any diabetic retinopathy changes were evaluated. Fasting blood sugar (FBS), post prandial blood sugar (PPBS) & HbA1c of each patient were considered as glycemic status markers. All the three parameters were correlated with superior, inferior, nasal, temporal & average RNFL thickness.

Using the spectral domain OCT in this study, we were able to detect significant decrease in inferior, superior and average RNFL thickness measurement in Type 2 diabetes without any clinical evidence of Diabetic retinopathy.

The Final Result:

1. Statistical correlation between FBS and RNFL thickness in different quadrants- P value is <0.001, hence the result is statistically significant (Table 4).
2. Statistical correlation between PPBS and RNFL thickness in different quadrants- P value is <0.001, hence the result is statistically significant (Table 5).
3. Statistical correlation between inferior RNFL thickness with HbA1c- P value is 0.0005, hence the result is statistically significant (Table 7).
4. Statistical correlation between superior RNFL thickness with HbA1c- P value is <0.001, hence the result is statistically significant (Table 8).
5. Statistical correlation between Nasal RNFL thickness with HbA1c- P value is 0.146, hence the result is statistically significant (Table 9).
6. Statistical correlation between Temporal RNFL thickness with HbA1c- P value is 0.7299, hence the result is statistically significant (Table 10).
7. Statistical correlation between Average RNFL thickness with HbA1c- P value is <0.001, hence the result is statistically significant (Table 11).

Our findings were in parallel to other studies done by Takahashi et al and Tekeli et al. In the study done by Tekeli et al, HRT was used to evaluate the optic nerve head parameter in diabetes mellitus with and without retinoscopy. Whereas Takahashi et al. used the stratus OCT which is different from tool compared with this study. Both studies did not find any significant reduction in RNFL thickness among the subjects of mild to moderate NPDR compared with age-related healthy subjects.

Our results were fairly similar to studies done by Lopes DE Faris et all and Takahashi et al which disclosed that RNFL was thinner in superior quadrant. This finding corroborates with previous study of Kern showing that the early events of Diabetic Retinal Disease (micro aneurysms and acellular capillaries) occur preferentially in the superior temporal quadrant rather than inferior area. Among the other studies Chung et al demonstrated that blood flow in the superior temporal retina increased in response to hypercapnia, but did not decrease in response to hyperoxia. In contrast, hyperoxia led to a decrease in blood flow to the inferior retina, whereas hypercapnia did not result in an increased blood flow within the area. The lack of normal vasoconstrictor response in this superior quadrant could explain why this region is more susceptible to micro aneurism acellular capillaries in diabetes mellitus and also why the retinal fiber is preferentially lost in this region even before clinically detectable diabetic retinopathy. Sugimoto postulated that the superior quadrant was more susceptible to under going damage compared with other areas and may have a tendency for higher rates of cell death, which result in RNFL thinning. Besides this it has come see that micro aneurysm present in this area and therefore less retinal nerve fiber layer damage occurred in this quadrant.

HbA1c is known as the index blood glucose in fasting and the postprandial state, and is well established and widely used as clinical measure of chronic glycemia. HbA1c of 6.5% has now been seen as sufficiently sensitive and specific to identify individuals who are the risk of developing diabetic retinopathy. From our study we noted that the

Volume 7, Issue 1; January-February 2024; Page No 164-178

majority of our subjects in diabetic patients without retinopathy changes had poor glycemic control. The HbA1c is greater than or equal to 6.5%. The result of mean HbA1c were fairly consistent with others.

Summary:

1. This was a cross sectional, hospital-based study to evaluate the Retinal Nerve Fiber Level (RNFL) thickness & Central Macular thickness (CMT) in type 2 diabetic patients without clinical diabetic retinopathy by Spectral Domain Optical Coherence Tomography (SD-OCT).
2. 80 eyes of 40 diabetic patients were selected fulfilling inclusion criterion and evaluated at Department of Ophthalmology, Dristideep Eye Hispital.
3. RNFL thickness was measured along a 3.4 mm circle entering the optic nerve head and CMT was measured along HD 5-line raster by SD-OCT.
4. Significant decrease in inferior, superior and average RNFL thickness measurement in TYPE 2 diabetic patients without any clinical evidence of diabetic retinopathy.
5. No significant change in the nasal and temporal RNFL thickness.
6. The decrease in the thickness in the superior, inferior and average RNFL thickness is affected by raised HbA1c level, raised fasting blood sugar (FBS) & PPBS level.
7. Using the spectral domain OCT in this study, no significant in CMT in relation to oxidized LOW Density Lipoprotein (LDL) levels were observed in Type 2 Diabetes patients without any clinical evidence of Diabetic Retinopathy.

Conclusion:

The Final result are:

1. Statistical correlation between FBS and RNFL thickness in different quadrants- P value is <0.001, hence the result is statistically significant.
2. Statistical correlation between PPBS and RNFL thickness in different quadrants- P value is <0.001, hence the result is statistically significant.
3. Statistical correlation between inferior RNFL thickness with HbA1c- P value is 0.0005, hence the result is statistically significant.
4. Statistical correlation between superior RNFL thickness with HbA1c- P value is <0.001, hence the result is statistically significant.
5. Statistical correlation between Nasal RNFL thickness with HbA1c- P value is 0.146, hence the result is statistically significant.
6. Statistical correlation between Temporal RNFL thickness with HbA1c- P value is 0.7299, hence the result is statistically significant.
7. Statistical correlation between Average RNFL thickness with HbA1c- P value is <0.001, hence the result is statistically significant.

Limitations:

There are certain limitations of our study. Main drawback of our study is sample size. The result of the study can be improved by increasing the sample size. Also, the patient are poorly characterized in aspects of several factors such as age, duration of diabetes, types of treatment whether the patient receives no treatment/oral hypoglycemia agents/insulin/lipid lowering agents or coexistent disease.

Also, it helps in qualitative assessment of decrease of RNFL, a quantitave result for an age matched population cannot be determined.

The duration of diabetes is also variable and further clarification is needed for the clarification is needed for the relation of outcomes in relation to duration of diabetes.

Reference:

1. 1. M. Rema & R. Pradeepa. Diabetic retinopathy: An Indian perspective. Indian Med Res 125, March 2007, pp 297-310
2. Raman R et al Prevalence of diabetic retinopathy in India: Sankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study report 2. Ophthalmology. 2009 Feb;116(2):311-8. doi: 10.1016/j.ophtha.2008.09.010. Epub 2008 Dec 12. Guidelines.
3. Williams R, Airey M, Baxter H. Epidemiology of Diabetic Retinopathy and Macular edema: A systemic review. Eye 2004; 18: 963-83.
4. Malone JI, Morrison AD, Pavan PR, Cuthbertson DD. Diabetic Control and Complication Trial: Prevalance and significance of retinopathy in subjects with type 1 diabetes

Volume 7, Issue 1; January-February 2024; Page No 164-178

of less than 5 years duration screened for the Diabetes Control and Complication Trial. Diabetes Care 2001; 124: 522-6.
5. Kohner EM, Aldington SJ, Stratton IM. United Kingdom Prospective Diabetes Study, 30: Diabetic retinopathy at diagnosis of non- insulin dependent diabetes mellitus and associated risk factors. Aech Ophthalmol 1998; 116: 297-303.
6. Rema M., Ponnaiya M., Mohan V. Prevalance of retinopathy in non-insulin dependent diabetes mellitus at a diabetes centre in southern India. Diabetes Res Clin Pract 1996; 34:29-36.
7. Sharma RA. Diabetic Eye disease in southern India. Community Eye Health 1996; 9:56-8.
8. Wild 5, Roglic G, Green A. Global prevalence of for the year 2000 and projections for 2030. Diabetes Care 2004; 27; 1047-53.
9. Dandona L, Dandona R, Naduvilath TJ, Population based assessrnent of diabetic retinopathy in an urban population in southern India. Bridiabetic Ophthalmo11999; 83: 937-.40.
10. 10. Larsen ML., Weirder M, Mogensen EF (1990). "Effect of long-term monitoring of glycosylated haemoglobin levels in insulin-dependent diabetes mellitus". N. Engl.J. Med. 323 (15): 1021-5.
11. Chew EY, Klein ML, Ferris FL 3rd, Remaley NA, Murphy RP, Chantry KHoogwerf BJ, Miller D: Association of elevated serum lipid levels with retinal hard exudate in diabetic retinopathy: Early Treatment Diabetic Retinopathy Study (ETDRS) report 22. Arch Ophthalmol 114:1079-1084, 1996.
12. Wu H, de Boer JF, Chen TC. Reproducibility of retinal nerve fiber layer thickness measurements using spectral domain optical coherence tomography. J Glaucoma. 2011 Oct;20(8).
13. Feuer WJ, Budenz DL, Anderson DR, Cantor L, Greenfield DS, Savell J,
1. Schuman JS, Varma R. Topographic differences in the age-related changes in the retinal nerve fiber layer of normal eyes measured by Stratus optical coherence tomography. J Glaucoma. 2011 Mar;2011.
14. Bagga, Greenfield DS, Feuer W, Knighton RW. Scanning laser polarimetry with variable corneal compensation and optical coherence torxography in normal and glaucomatous eyes. Am J Ophthalmol. 2003 Apr; 135(4):521-9.
15. Kim HG, Heo H, et al. Comparison of scanning laser polarimetry and optical coherence tomography in preperimetric glaucoma. Optom Vis Sci. 2011 Jan;88(1):124-9.
16. Williams textbook of endocrinology (12th ed.). Philadelphia: Elsevier/Saunders. pp. 1371-1435.
17. Wild S, Roglic G, Green A, Sicree R, King H (2004). "Global prevalence of diabetes: Estimates for the year 2000 and projections for 2030". Diabetes Care 27 (5): 1047-53.
18. Gale, Jason (November 7, 2010). "India's Diabetes Epidemic Cuts Down Millions Who Escape Poverty".
19. Indian Heart Association Why South Asians Facts Web. 30 April 2015
20. Gale, Jason (November 7, 2010). "India's Diabetes Epidemic Cuts Down Millions Who Escape Poverty".
21. Kleinfield, N. R. (September 13, 2006). "Modern Ways Open India's Doors to Diabetes". New York Times.
22. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Geneva, World Health Organization, 1999 (WHO/NCD/NCS/99.2).
23. Wolff E. The anatomy of the eye and orbit. Philadelphia, Blakiston, 1948.263
24. Curcio CA, Allen KA. Topography of ganglion cells in human retina. J Comp Neuro1.1990; 300(1):5-25.
25. Linden R. Displaced ganglion cells in the retina of the rat. J Comp Neurol. 1987; 258(1):138-143.
26. Ogden TE. Nerve fiber layer of the macaque r tinotopic organization. Invest Ophthalmol Vis Sci. 1983; 24(1):85-98.
27. Minckler DS. The organization of nerve fiber bundes in the primate optic nerve head. Arch Ophthalmol. 1980; 98:1630.
28. 546. Hoyt WF, Luis O. Visual fiber anatomy in the infrageniculate pathway of the primate. Arch Ophthalmol. 1962; 68:94.

Volume 7, Issue 1; January-February 2024; Page No 164-178