"RELATIONSHIP BETWEEN GLYCOSYLATED HEMOGLOBIN LEVELS AND MACULAR THICKNESS ON OPTICAL COHERENCE TOMOGRAPHY IN TYPE II DIABETIC PATIENTS"

By

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MBBS

Dissertation submitted to the

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCHCENTRE, KOLAR

In partial fulfillment of the requirements for the degree of

MASTER OF SURGERY

IN

OPHTHALMOLOGY

Under the guidance of

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JUNE/JULY 2023

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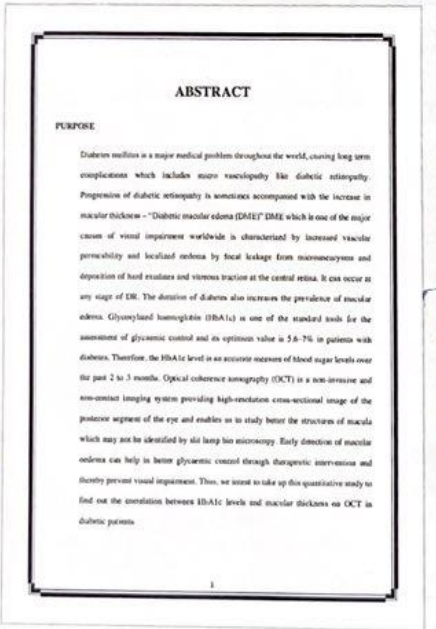

ABSTRACT

PURPOSE

Diabetes mellitus is a major medical problem throughout the world, causing long term complications which includes micro vasculopathy like diabetic retinopathy. Progression of diabetic retinopathy is sometimes accompanied with the increase in macular thickness - "Diabetic macular edema (DME)" DME which is one of the major causes of visual impairment worldwide is characterized by increased vascular permeability and localized oedema by focal leakage from microaneurysms and deposition of hard exudates and vitreous traction at the central retina. It can occur at any stage of DR. The duration of diabetes also increases the prevalence of macular edema. Glycosylated haemoglobin (HbA1c) is one of the standard tools for the assessment of glycaemic control and its optimum value is 5.6-7% in patients with diabetes. Therefore, the HbA1c level is an accurate measure of blood sugar levels over the past 2 to 3 months. Optical coherence tomography (OCT) is a non-invasive and non-contact imaging system providing high-resolution cross-sectional image of the posterior segment of the eye and enables us to study better the structures of macula which may not be identified by slit lamp bio microscopy. Early detection of macular oedema can help in better glycaemic control through therapeutic interventions and thereby prevent visual impairment. Thus, we intend to take up this quantitative study to find out the correlation between HbA1c levels and macular thickness on OCT in diabetic patients.

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ACKNOWLEDGEMENT

One of the joys of completion of this dissertation is to look over the journey in the past and remember and thank all the people who have helped and supported me along this road.

I am deeply indebted and grateful to my guide, **DR. B. O. HANUMANTHAPPA**, Professor and Head of Unit, Department of Ophthalmology, Sri Devaraj Urs Medical College, for his able guidance, support, timely advice, and constant encouragement throughout the period of the study.

I thank **DR. MANJULA T.R**, Professor and Head of Department of Ophthalmology, for her constant support.

I would like to express my heartfelt thanks and deepest gratitude to my Associate Professors **DR. SANGEETHA T, DR. USHA B R, DR. RASHMI G**; my Assistant Professors, **DR. INCHARA N, DR. CHAITRA M C, DR. RESHMA R** and Senior Resident **DR. RAHUL GOWDA, DR NAVEENA** Sri Devaraj Urs Medical College Tamaka, Kolar, for their encouragement and suggestions during this study and post-graduation course. I thank all my teachers.

I express my deepest gratitude to **DR. SANDHYA R**, former Head of Department, Sri Devaraj Urs Medical College, and my former guide for her constant guidance.

My gratitude and thanks to **DR. P.N. SREERAMULU**, Principal, Sri Devaraj Urs Medical College Tamaka, Kolar, for letting me use the college and hospital facilities and resources.

My special thanks to **DR. AMULYA P, DR. ANNESHI R C, DR DEEPAK ARORA, DR KARISHMA, DR AASTHA, DR. APURVA NAVALE, DR. MONISHA** for their constant help and advice. I would also like to thank my batchmates **DR. SWATI, DR**

RAHEEMUNNISA, DR. POOJITHA, DR KRUTHIKA, DR YUGANDHARA, DR APARNA, DR RAMYA, DR YAMINI and DR PANAAH for all their help during this study and making my journey through it smooth. I would also like to thank my juniors **DR. PREETHI, DR DIVIJA, DR LEKSHMY, DR SAMEEKSHA, DR HITHESH, DR SANJANA, DR RAVEENA & DR ANUNITHA** and all my friends for their help and support.

I would like to thank my parents, **MR GHANSHYAM MALANI** and **MRS KALPANA MALANI** whose countless sacrifices and blessings have made me who I am today. Thank you for always being with me and giving me strength at every step of my life.

I would also like to thank my brother **DR SHUBHAM MALANI** and sister-in-law **DR KAMNA MALANI**, and my friends **DR VEDANTH, DR INDRANIL**, **MR PRANAV RATHI**, **DR KUNAL, DR SANKET, DR KHUSHBOO AND DR ANUP** for being my support in all the tough times.

Last but not the least, I thank all my patients involved in this study, without whose cooperation, this dissertation would have never materialized. I sincerely thank my institute Sri Devaraj Urs Medical College, Tamaka, Kolar for giving me a wonderful foundation and forum

Last, but not the least, I would like to express my gratitude to the Almighty for all his blessings.

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LIST OF ABBREVIATIONS

SL NO.	ABBREVIATION	FULL FORM
1.	T2DM	Type II Diabetes Mellitus
2.	DME	Diabetic Macular Edema
3.	DR	Diabetic Retinopathy
4.	OCT	Optical Coherence Tomography
5.	CSMT	Central Subfield Macular Thickness
6.	TMV	Total Macular Volume
7.	VEGF	Vascular Endothelial Growth Factor
8.	AGEs	Advanced Glycation End products
9.	T1DM	Type I Diabetes Mellitus
10.	BRB	Blood Retinal Barrier
11.	A-Scan	Amplitude Scan
12.	IGT	Impaired Glucose Tolerance
13.	WHO	World Health Organization
14.	NPDR	Non-Proliferative Diabetic Retinopathy
15.	PDR	Proliferative Diabetic Retinopathy
16.	CSME	Clinically Significant Macular Edema
17.	NVD	Neovascularization over Disc
18.	NVE	Neovascularization Elsewhere
19.	FFA	Fundus Fluorescein Angiography
20.	ICGA	Indocyanine Green Angiography
21.	TD-OCT	Time Domain Optical Coherence Tomography
22.	SD-OCT	Spectral Domain Optical Coherence Tomography
23.	OCT-A	Optical Coherence Tomography Angiography
24.	CME	Cystoid Macular Edema
25.	ARMD	Age Related Macular Degeneration

26.	RE	Right Eye
27.	LE	Left Eye

ABSTRACT

PURPOSE

Diabetes mellitus is a major medical problem throughout the world, causing long term complications which includes micro vasculopathy like diabetic retinopathy. Progression of diabetic retinopathy is sometimes accompanied with the increase in macular thickness – "Diabetic macular edema (DME)" DME which is one of the major causes of visual impairment worldwide is characterized by increased vascular permeability and localized oedema by focal leakage from microaneurysms and deposition of hard exudates and vitreous traction at the central retina. It can occur at any stage of DR.The duration of diabetes also increases the prevalence of macular edema.Glycosylated haemoglobin (HbA1c) is one of the standard tools for the assessment of glycaemic control and its optimum value is 5.6–7% in patients with diabetes. Therefore, the HbA1c level is an accurate measure of blood sugar levels over the past 2 to 3 months.Optical coherence tomography (OCT) is a non-invasive and non-contact imaging system providing high-resolution cross-sectional image of the posterior segment of the eye and enables us to study better the structures of macula which may not be identified by slit lamp bio microscopy.Early detection of macular oedema can help in better glycaemic control through therapeutic intervention and thereby prevent visual impairment.Thus, we intent to take up this quantitative study to find out the correlation between HbA1c levels and macular thickness on OCT in diabetic patients

AIMS AND OBJECTIVES

- To assess the relationship between HbA1c levels and macular thickness in type 2 diabetic patients.

MATERIAL AND METHODS

A cross sectional study conducted in Department of Ophthalmology in R.L.J Hospital and Research Centre attached to Sri Devaraj Urs Medical College from January 2021 and September 2022. A total of 162 eyes of 52 males and 29 females were evaluated. After obtaining consent, demographic details were noted & then subjected for detailed ophthalmic examination of both eyes including Visual acuity, Slit lampbio microscopy, IOP by Goldman Applanation Tonometry, Fundus examination, CSMT and Total Macular Volume by OCT and HbA1c levels.

RESULTS

Mean age of the patients was 59.36 years. While comparing the subfield thickness in between right eye and left eye, non-significant results were obtained. Mean macular volume among the left and right eye were found to be 9.65µm and 9.85µm respectively. On comparing statistically, the results were found to be statistically significant. Significant positive correlation was observed between central subfield thickness (Central, Nasal, Temporal) and HbA1c among both left and right eyes. Significant positive correlation was observed between

total macular volume and HbA1c among both left and right eyes. No significant association was observed between the eye and grade of retinopathy. No significant association was observed between the eye and grade of retinopathy

CONCLUSION

Our results provide population-based data that would be useful in the interpretation of macular thickness values in persons with diabetes. Current results demonstrate that macular thickness measurements are increased in moderate or severe DR even when diabetic macular oedema is absent.

Key words: Macular thickness, Diabetic macular edema, Diabetic Retinopathy, Hba1c, OCT

TABLE OF CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

LIST OF PHOTOS

INTRODUCTION

RELATIONSHIP BETWEEN GLYCOSYLATED HEMOGLOBIN LEVELS AND MACULAR THICKNESS ON OPTICAL COHERENCE TOMOGRAPHY IN TYPE II DIABETIC PATIENTS

In new era, diabetes mellitus has been an epidemic on a global scale. Over the next ten years, there would be over two hundred million individuals having diabetes worldwide, most of whom have T2DM. Also, all of them are likely to show complications, claims World Health Organization.[1, 2] Chronic hyperglycaemia is a hallmark of a broad spectrum of diseases known collectively as type 2 diabetes mellitus, which are lead by a variety of environmental as well as genetic risk variables. [3, 4]Population explosion, rising senior population, cost of industrial growth, urban trend, preference for high-fat junk food, sedentary lifestyle, and obesity are further correlates. [5, 6]

The most logical course of action appears to be early clinical attention in the prediabetes period to prevent problems in order to alleviate the enormous public health and economic burden caused by the pandemic of T2DM.[4] It has been demonstrated that sensible lifestyle adjustments significantly lower the likelihood of progression among those having abnormal fasting glucose (IFG). [5] In T2DM, the age-adjusted death rates are one and half percent to two and half percent higher than in the standard population. Among high-, middle-, as well as low-income nations, a newer systematic review as well as meta-analysis revealed a correlation between increased risk of T2DM with lower levels of education, occupation, and socioeconomic position. [6]

DM complications are often the result of long-term exposure to enhanced and extremely elevated glucose values in the blood brought on by abnormalities of metabolic activities of insulin. A highly significant cause of illness as well as fatality across the globe is quickly evolving to include DM and its complications. In both wealthy and underdeveloped nations, the DM pandemic has spread quickly. It is anticipated that DM will become an epidemic in the not-too-distant future. More than two hundred forty million individuals around the world are impacted by DM, and by 2030, this value is anticipated to increase to over 370 million. Glaucoma, cataracts, ocular surface disorders, diabetic retinopathy, and diabetic papillopathy are just a few of the ocular problems that can result from DM. [7]

The retina seems to be a slim coating of tissue located close to optic nerve in back of the eye. It's a crucial component responsible for vision as well as injury to it may have disastrous repercussions since it comprises a sheath of photoreceptors as well as transforms the light from lens into neural impulses. The macula consists of highest quantity of rods(along with cones). DM may cause edema of macula through a variety of ways. Among the primary reasons for visual disturbance in the US is this.[8, 9]

AGEs are created because of hyperglycaemia and diabetes. The precise cause of diabetic retinopathy is unknown, however it is likely the result of numerous interrelated events. Osmotically active AGEs could be to blame for the fluid buildup in the macula. The barrier between the blood and the retina is also disrupted due to diabetes, which is probably a chiefelement in the establishment of diabetic associated macular edoema. Additionally, AGEs

are linked to elevated levels of inflammatory markers like protein kinase C, VEGF, and leukocyte adhesion.[10, 11]

In the world, DME (diabetic macular edema) is among the primary factors contributing to visual loss. According to some research, macular edema affects almost 1 in 3 patients with diabetes. People having T1DMare prone to acquire DME than people having T2DM. The incidence of DME among subjectshaving diabetes over the period of 10 years is roughly 20% in those detected earlier thanthirty years of age as well as roughly forty percent in those detectedafter thirty years of age. Within 9 years of the onset of diabetes, 27% of individuals show symptoms of macular edema, according to another study. Numerous research that focus on various demographics show that DME is becoming more common. [12,13]

The disruption of the BRB is secondary to the pathogenesis of diabetic macular edoema. The ophthalmic vasculature is separated from the retina's photoreceptors by the BRB. The BRB operates in a complicated manner involving numerous coexisting components, although most of the physiological mechanisms are not well comprehended. An outer and an inner barrier are the two main compartments that make up the BRB. The disruption of both compartments' permeability following the onset of diabetes has been demonstrated in animal models. Macular edoema builds up when this barrier is disrupted, but the procedure is highly involved as compared to this as well as also includes a number of inflammatory indicators that are increased due to AGEs, hyperglycemia, as well as diabetes. Vasoconstriction brought on by diabetes increases VEGF expression. Macular is another outcome of VEGF. It also leads to macular edema as well as vasculogenesis, that causes further retinal disorder.[14, 15]

Visual loss is frequently caused by macular oedema. However, it has frequently been noted in clinical practise that having macular oedema is not a need for having clear vision. According to research by Nussenblatt et al, there exists a stronger association among macular thickness as well as visual acuity than macular oedema. Slit lamp bio microscopy, stereoscopic photography as well as fluorescein angiography constitute the examples of conventionalprocesses for evaluating macular oedemawhich are highly qualitative as well ascomparatively insensitive to slight alterations in retinal thickness. Since the establishment of OCT (optical coherence tomography), it's been easier for the doctors to evaluate the efficiency of severaltreatmentapproaches as well as consistently detect as well asestimate slightmodificationsin retinal thickness.[16]

With the help of OCT, we can study the macula's structures more thoroughly. These structures might not be visible with slit lamp bio microscopy. Low coherence interferometry is used in OCT in order to provide cross-sectional scans of retina. It makes use of infrared light which is split among 2 components: First component is reflected via a reference mirror and second which is dispersed by biological tissue.[17]

One of the common tests for measuring glycaemic management is glycosylated haemoglobin (HbA1c), which has an ideal range of 5.6–7% in diabetic individuals. The HbA1c value is a definitive indicator of blood sugar concentrations during the past two to 3 months. Through therapeutic intervention, early diagnosis of macular oedema can improve glycaemic management and hence avert visual damage. [16, 17]

Therefore in context to the aforementioned information, the current research was carried out for evaluating the relationship between glycosylated hemoglobin levels and macular thickness on optical coherence tomography among T2DM subjects.

AIMS AND

OBJECTIVES

- To assess the relationship between HbA1c levels and macular thickness in type 2 diabetic patients.

REVIEW OF LITERATURE

ANATOMY OF EYE

The eyeball is a cystic framework that is constantly inflated by internal pressure. It is formed by the fusion of 2 altered spheres.

The eyeball is curved in the front as well as back. The anterior as well as posterior poles, which are located at the Centre of the curvatures with the greatest convexities, are referred to as such. The adult eyeball has a perimeter of seventy-five millimeters as well as a capacity of six and a half milliliters. The average adult eye weighs seven grammes. [18, 19]

COATS OF EYEBALL

It is composed of three structural complements – Fibrous layer which is present on the outermost surface, a vascular layer in the centre and a nerve layer on the innermost side.

1. FIBROUS COAT- It is a small, sturdy wall that shields eye. The corneais the transparent portion of external layer. Sclera is the opaque portion of the posterior five sixth of the eye. Limbus refers to the intersection of the sclera as well as cornea.

2. VASCULAR COAT- this layer of eye is known as Uveal tissue that provides nutrition to several components of eye.

It is segregated into 3 structures - a) Iris

b) Ciliary Body

c) Choroid

3. NERVOUS COAT- internal nervous layer is known as Retina. It carries out visual roles as well as through visual channel, it projects to visual cortex. [18, 19]

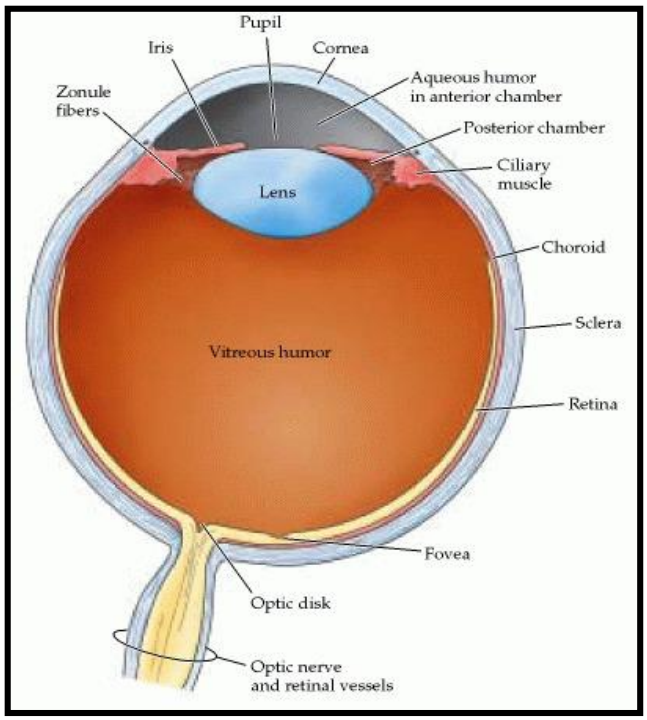
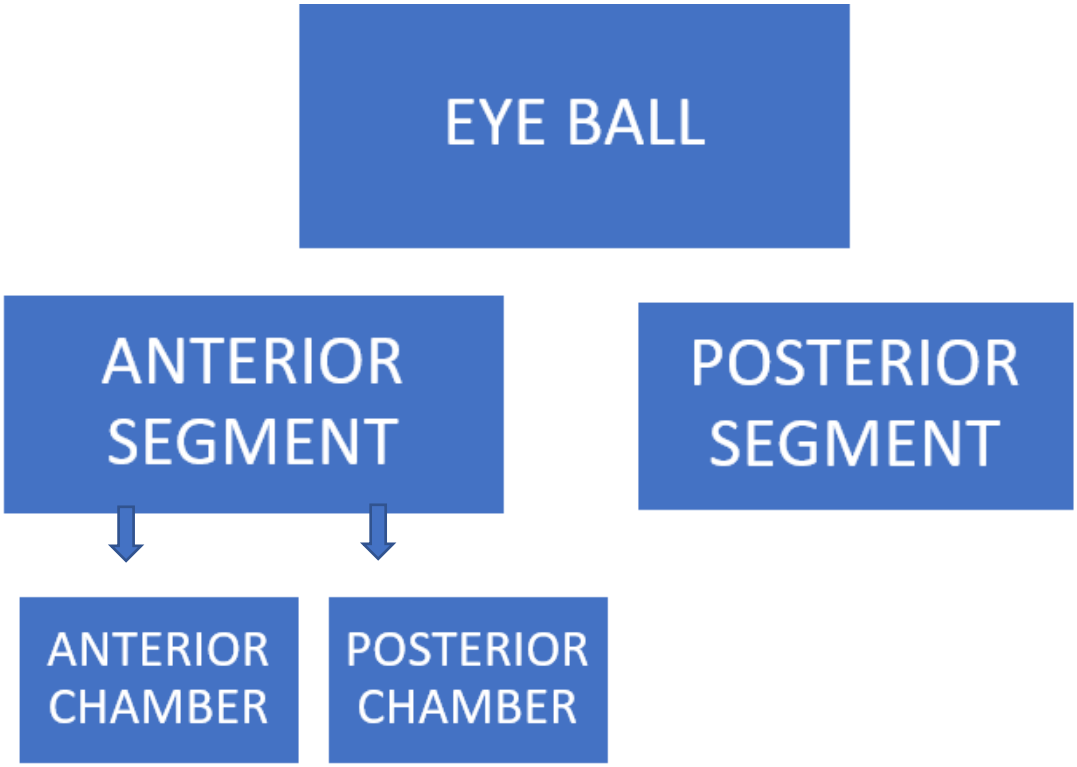


Figure 1: Anatomy of eye

SEGMENTS AND CHAMBERS

It is segregated into 2 sections by Iris.



a) ANTERIOR SEGMENT- involves cornea, anterior chamber, iris, lens as well as posterior chamber.

b) **POSTERIOR SEGMENT –** It involves the components situated behind lens, which include vitreous humor, retina, choroid as well as the optic disc.[18, 19]

ANATOMY OF RETINA

Incoming photons are captured by the retina and are then transmitted along neural channels as electrical as well as chemical impulses for the cortex to interpret a visual image. The retina makes up the innermost barrier between the vascular choroid as well as the fibrous sclera, is situated in the rear section. At various periods of life, the retina can have pathological symptoms, most of which seriously impair vision and, as a result, value of life.

Structure and Function

The topics mentioned below are related to the morphology as well as functioning of retina :

- Photoreceptor cells
- Layers of the retina
- Macula

STRUCTURE

Photoreceptor Cells[20]

Rod as well as cone photoreceptor cells are specifically found farther from the pupil. Rods are found on the retina's edge as well as are highly reactive in reduced illumination. In the daytime, cones are highly responsive as well as may absorb different colour light wavelengths. The fovea, in the middle of the retina, is where cones localise. The retina has over a hundred million rods as well as around six million cones. Tritans, Deutrans, as well as

Protans are 3 different cone types that are distinguished by their ability to recognize short, medium, as well as long wavelengths, correspondingly.

Every form of cone cell may be distinguished as recognizing blue, green, as well as red wavelengths when it comes to colour vision. The human eye perceives the visible light spectrum as an outcome of the 3 kinds of cones' perceptible wavelength spectrum overlap. Rhodopsin, a pigment formed of retinal which is responsive to light and enables photon absorption, is a component of rod cells. Vitamin A is a crucial nutritional element for the promotion of the phototransduction process since retina is an aldehyde of vitamin A. A substantial risk element for juvenile blindness i.e. vitamin A insufficiency is still widespread in underdeveloped areas like South Asia as well as sub-Saharan Africa. [20]

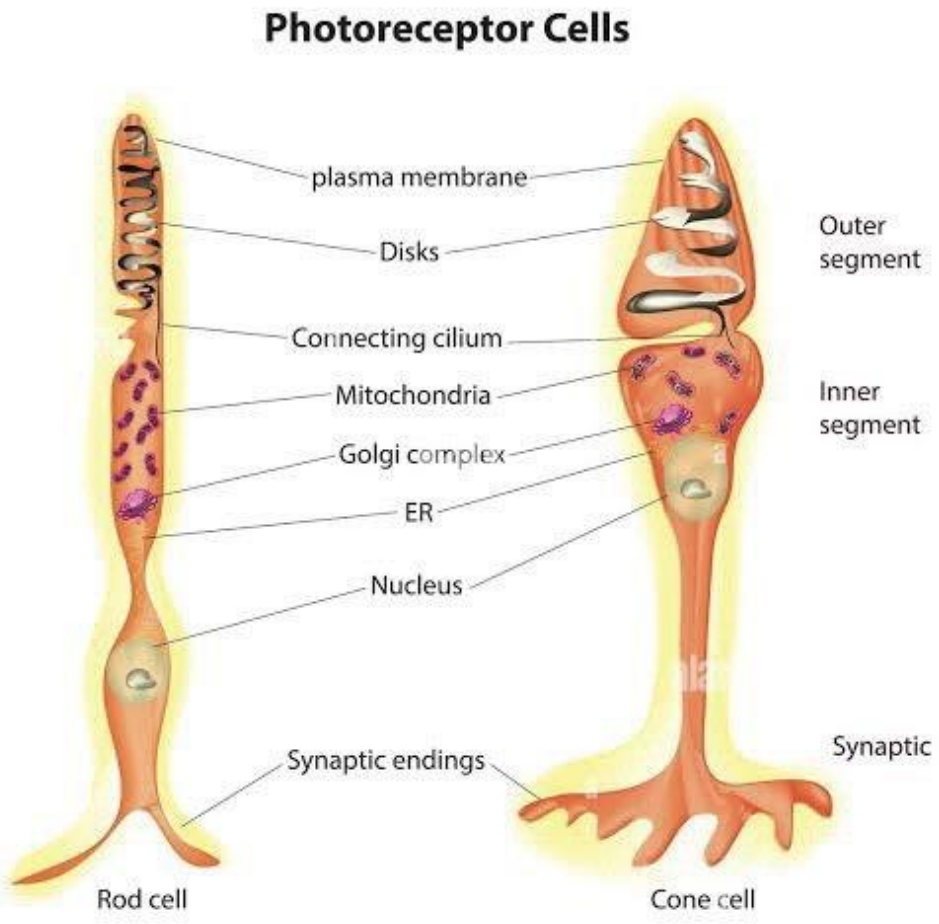


Figure 2: Photoreceptor cells

Layers of the Retina[20]

The retina is divided into 10 different layers which are demonstrated in sequence from the internal most coatings nearer to pupil to the coatings situated towards posterior as well as at the boundary of eyeball:

- **Inner Limiting Membrane** – a smooth barrier between the retina's innermost layer and the vitreous humour, that occupies the eye's vitreous chamber. Müller glial cells make up this layer's periphery as well as serve to preserve retinal equilibrium by reinforcing other cells as well as preserving retinal lamination.

- **Retinal Nerve Fiber Layer** –Muller cell projections with combination of astrocytes as well as retinal ganglion cell axons form this layer. The cells of basal lamina of this layer are those of the internal limiting membrane.

- **Ganglion Cell Layer** – consists of ganglion cell entities projecting their axons, ultimately to develop the optic nerve.

- **Inner Plexiform Layer** – The bipolar cells' axons connect to the ganglion cells in this layer. Amacrine cell dendrites also form synapses in this area and have the role of controlling the electrical transmission among ganglion cells as well as bipolar cells, limiting lateral potentiation.

- **Inner Nuclear Layer** – the layer made up of the amacrine, horizontal, as well as bipolar cells' cell components. Bipolar cells serve as pathways which propagate as well as process different synaptic impulses onto ganglion cells originating from

photoreceptor cells. Rod as well as cone cells receive feedback control from horizontal cells.

- **Outer Plexiform Layer** –the area where dendrites of cells in the innermost nuclear membrane interact with terminals of photoreceptor cells.
- **Outer Nuclear Layer** – consists of the cell entities of both rods as well as cones.
- **External Limiting Membrane** – the portion which is made up of gap junctions among Muller cells as well as photoreceptor cells; it divides the rod as well as cone cell structures into their internal as well as external sections.
- **Photoreceptor Layer –** the area where the internal as well as external sections of rods as well as cones meet. The light-reactive pigments required for phototransduction, like rhodopsin, are found in membrane-bound discs which make up the external photoreceptor sections. The internal sections contain a large number of mitochondria necessary to satisfy the photoreceptor cells' high metabolic needs.
- **Retinal Pigment Epithelium** – the outermost covering of the retina which is only one cell wide. It also performs a variety of other tasks, such as ion as well as water transport & growth factor as well as cytokine production. The exterior sections of the rods as well as cones interact with the RPE cells. Due to this close contact, all-trans-retinal can be recycled into 11-cis-retinal as well as delivered back to the cones as well as rods for phototransduction. Both photoreceptor cells as well as the accompanying capillary endothelium depend on RPE cells for support as well as maintenance. [20]

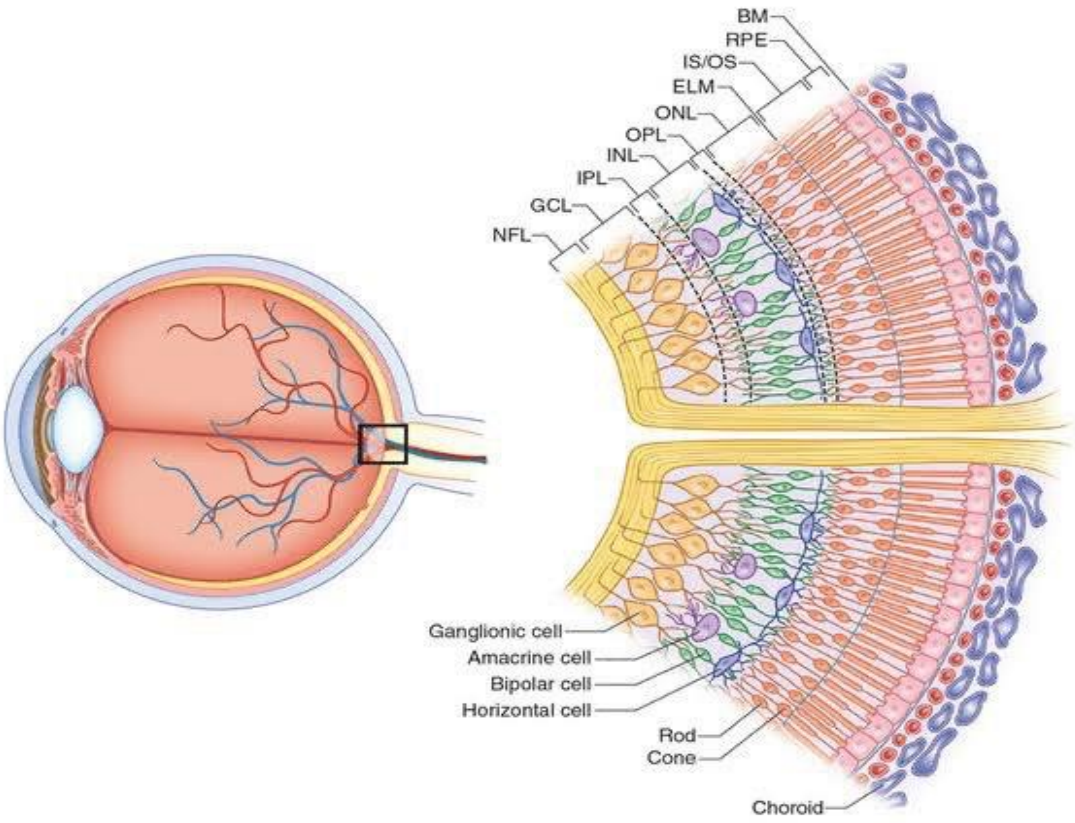


Figure 3: Layers of retina

Anatomy of Macula

The macula, generally known as the macula lutea due to its yellowish pigmentation, is the highly delicate region of the retina and provides the maximum level of visual clarity. In a fundoscopic investigation, it is discovered temporally from the optic disc. The carotenoids which constitute the macular pigments as well as impart them their yellowish shade are lutein as well as zeaxanthin. Such pigments are well known for their ability to screen blue light as well as possess anti-inflammatory effects. Lutein as well as zeaxanthin supplementation have been demonstrated to improve pigment concentration as well as is linked to a lower incidence of diabetic retinopathy in grownups and preterm birth retinopathy in newborns. The fovea, an avascular dip in the macula's center that houses a significant number of cones, is located there.

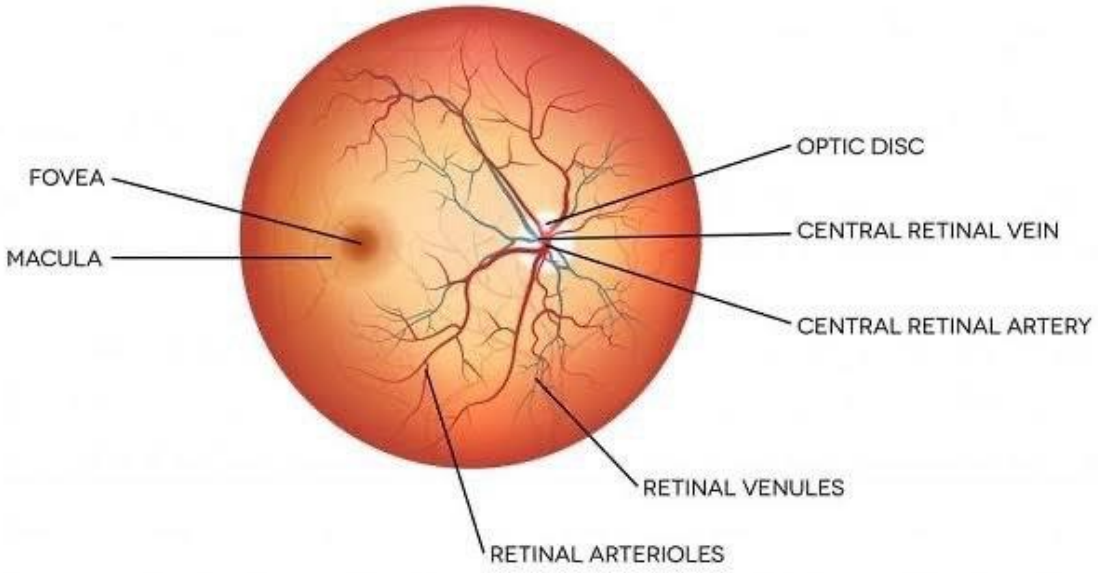


Figure 4: Normal Fundus picture

The macula has been subsequently divided into progressively smaller circular regions which are characterized by a reduction in rod density as well as a reduction in the number of cell coats surrounding photoreceptor cells: [20]

- Perifovea
- Parafovea
- Fovea
- Foveal avascular zone
- Foveola
- Umbo

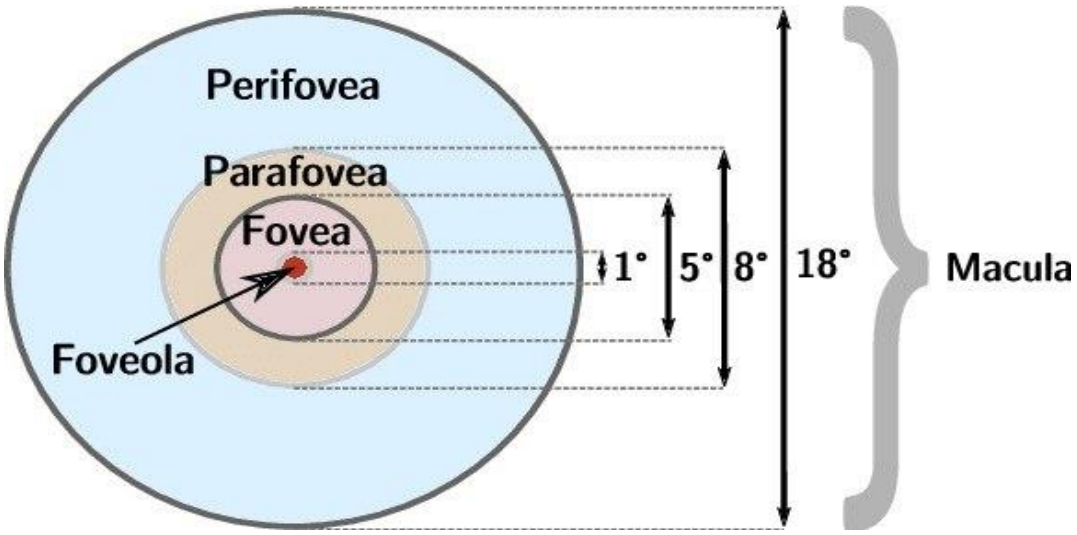


Figure 5: Anatomy of Macula

The Foveola:

Even though it covers a little portion of the visual field i.e., 1°, the foveola, that has dimensions of 0.35 millimeters in diameter as well as 0.13 millimeters in width, is the region of the retina with the maximum degree of visual clarity. This is explained by the fact that only cone photoreceptors are present, as well as by the fact that it is not vascularized. Because the choriocapillaris, that illuminates via the foveola, has strong choroidal circulation, it generally seems deeper red as compared to the surrounding retina. In instances of central retinal vascular impairment as well as in some metabolic storage disorders, the color of the fovea remains and is enhanced as the 'cherry-red spot' once the surrounding retina turns hazy.[20]

BLOOD SUPPLY AND LYMPHATICS

The retina is vascularized by blood vessels as well as the choroid. The choroid provides the retina's external layers, and its internal layers are supplied by branches of large blood vessels. Following are the details of each vessel which contributes to retina’s vasculature.

Central Retinal Artery – Principal blood artery which feeds the retina's internal layers; it passes through optic nerve sheath. The superior as well as inferior arcades of central retinal artery will eventually create the blood-retina barrier. A significant branch of the ocular artery is where it starts.

Central Retinal Vein – the primary drainage system for the retina, which passes inside the optic nerve's sheath together with the major retinal artery.

Long Posterior Ciliary Arteries – Near the optic nerve entrance region, these 2 arteries emerge from the ophthalmic artery and then penetrate the sclera.

Short Posterior Ciliary Arteries – These vasculatures arise from ophthalmic artery as a couple branches, then divide into ten to twenty tiny blood vessels which pierce the posterior sclera as well as surround optic nerve. Optic cup is nourished by the circle of Zinn. The Bruch membrane as well as external retina are additionally supplied by posterior ciliary arteries.

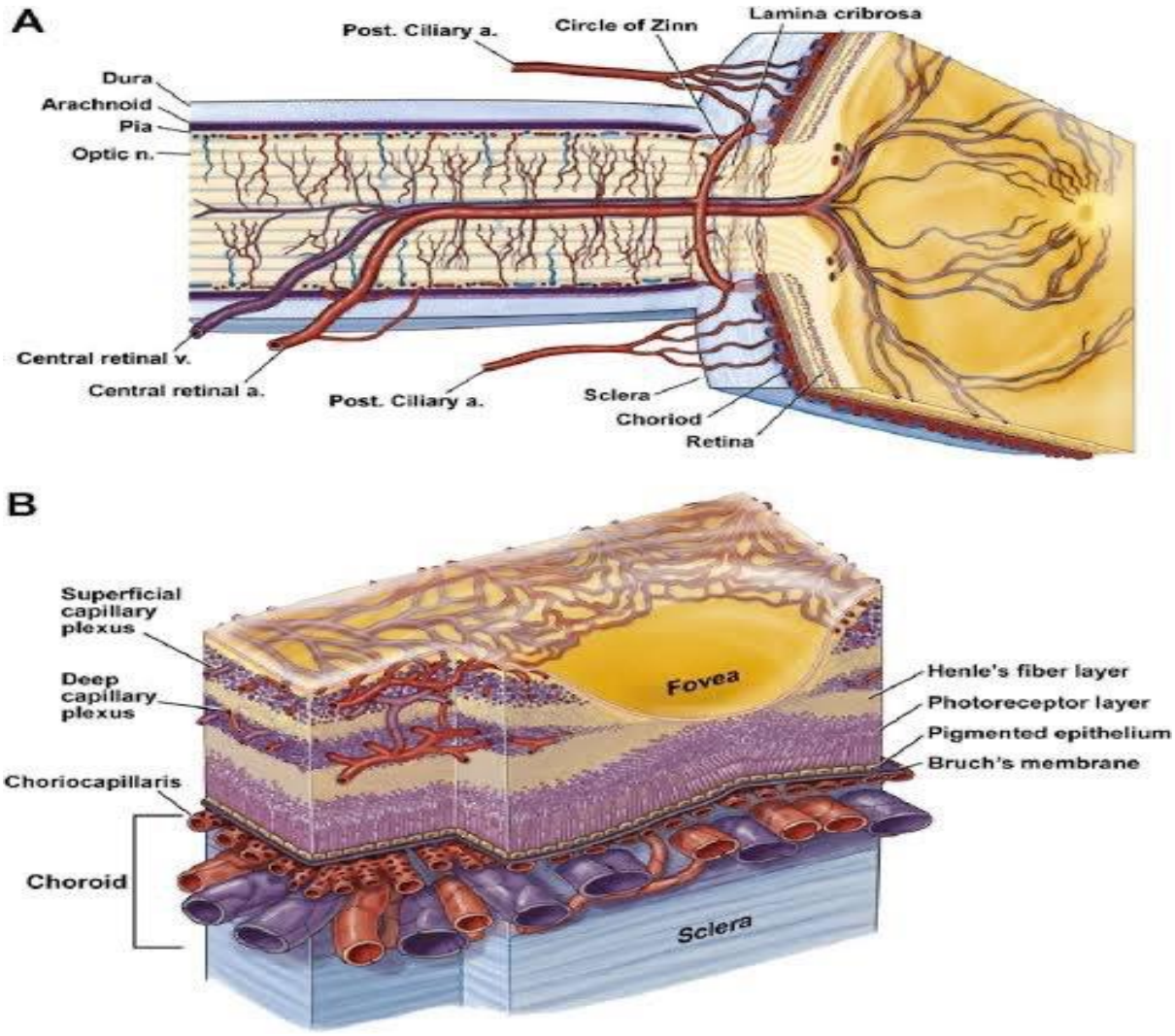


Figure 6: Vasculature of Retina

Choroid –2nd principal layer, also known as the tunic of eye. Choriocapillaris is thickest behind the fovea as well as gets thinner as it moves outward. No lymphatic vessels in the retina are observed.[21]

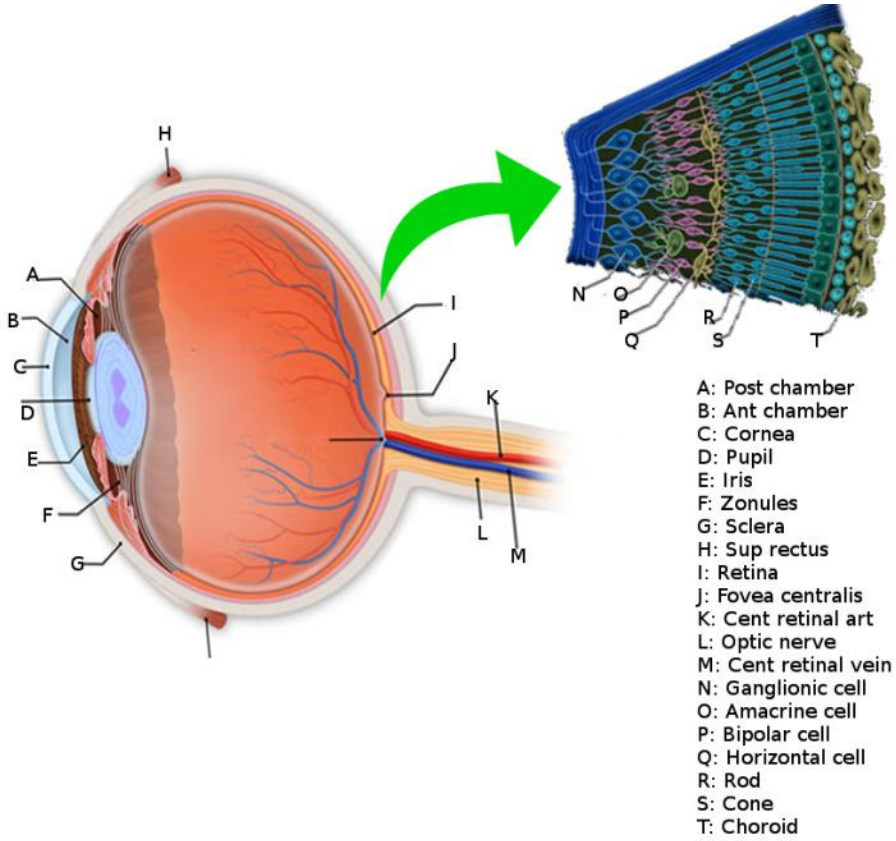


Figure 7: Anatomy of Eye and Retina

DIABETES MELLITUS

Chronic hyperglycemia accompanying disruptions of the metabolism of carbohydrates, fats, as well as proteins are the hallmarks of this category of metabolic illnesses, which can be caused by an absolute or relative lack of insulin production or activity. Diabetes affects a variety of organs over the long term, particularly the eyes, renal tissue, neural tissue, cardiac tissue.[22- 24]

The American Diabetes Association's expert committee as well as the WHO have collaborated to propose revised classification as well as diagnostic parameters.[2] Because of the ambiguity of such words, patients are typically categorized according to their therapy instead of their aetiology. [22- 24]

EPIDEMIOLOGY

According to the Diabetes Atlas 2012, there are three hundred and seventy-one million persons having diabetes globally, and the occurrence rate is 8.3 percent. India will become the "Diabetes Capital" of the globe by 2030. According to WHO standards, the occurrence rate of confirmed diabetes was 5.6 percent in urban regions as well as 2.7 percent in remote ones. Maharashtra's status is like other states. The occurrence rate has spiked from 1.5 percent in 1963 to 9.3 percent in 2001 in Mumbai's urban region, as well as from 3.9 percent in 1991 to 9.3 percent in 2006 in the remote region. Latest data from the IDF's Diabetes Atlas

shows that sixty-five million individuals in India have diabetes, making about seventeen percent of the world's diabetic community.[25, 26]

In 2014, the WHO predicted that eight and a half percent of individual aged above eighteen years had diabetes globally. The occurrence rate in remote locations seemed to be ranging from three percent to roughly eight percent among community ranging in age of twenty years or beyond, with a somewhat increased prevalence among people beyond fifty years of age. The incidence in urban sectors varies from 10.9 to 14.2 percent.[25, 26]

The IDF has been documenting prevalence of DM at the local, national, as well as international levels since 2000. Two hundred and eighty-five million people were thought to have diabetes in 2009. This number rose to three hundred and sixty-six million in 2011, three hundred and eighty-two million in 2013, four hundred and fifteen million in 2015 as well as four hundred and twenty five million in 2017. By 2030, the predicted worldwide burden will reach five hundred and fifty-two million. [25, 26]With 1.3 billion people, India has the second-highest population in the world and the highest occurrence rate of diabetes i.e., 7.8 percent. [25, 26]

ETIOLOGICAL CLASSIFICATION - DM[22- 24]

Type 1

Auto immune

Idiopathic

Type 2

Predominantly insulin Resistance

Predominantly insulin secretory defects

Other Specific Types

- Genetic anomalies of beta cell malfunction e.g., MODY 1 to 4
- Genetic anomalies in insulin activity e.g., Type A insulin resistance
- Disorders of Exocrine pancreas, e.g., Fibro calculus pancreatopathy
- Endocrinopathies, e.g., Acromegaly, Cushings, etc.,
- Drugs or chemical induced, e.g., glucocorticoids Infections, e.g., congenital rubella
- Rare types of immune mediated diabetes, e.g., Stiff Man Syndrome
- Other genetic disorders[22- 24]

STAGES OF DIABETES[22- 24]

The full spectrum involves cases of type 1 diabetes. There may be a time during the initial phases of treatment when no insulin is needed, however subsequently, insulin is necessary for survival. Insulin might be necessary in type 2 diabetes after a stage of ketoacidosis brought on by extreme stress or an illness.

DIAGNOSIS of DM[22- 24]

a) DM is detected when the fasting value is equal to or more than one hundred and twenty-six milligrams or a two-hour plasma glucose is equal to or over two hundred milligrams.
b) Impaired Glucose Tolerance is observed if fasting glucose comes out to be less than or equal to one hundred and twenty-six milligrams as well as if the 2-hour score varies from one hundred and forty to two hundred milligrams per decilitre.
c) Impaired fasting glucose is noticed if the fasting glucose is more than or equal to one hundred milligrams and 2-hour value is less than or equal to one hundred and forty milligrams per decilitre.
d) Glucose Tolerance is normal if the fasting as well as the two-hour scores are below one hundred milligrams as well as one hundred and forty milligrams per decilitre accordingly.
e) Diagnostic parameters for gestational DM are different.

COMPLICATIONS OF TYPE II DIABETES

Diabetes is a condition which is firmly linked to both microvascular as well as macrovascular complications. Physical therapists may progressively confront individuals having prediabetes, initial type 2 diabetes without or with merely a few vascular issues, as well as more severe condition with numerous vascular consequences due to the continuous pattern of the condition.[27]

Anatomical, morphological as well as functional modifications to the vascular system caused by diabetes can contribute to multiorgan failure. Physical therapists are progressively becoming first-line suppliers of intervention for musculoskeletal as well as mobility abnormalities in individuals with diabetes. These therapists will also be crucial in the treatment of diabetics considering the multiple therapies they may offer that can help with symptom relief, decrease the metabolic development to overt type 2 DM, as well as minimize the morbidity as well as fatality linked to such problems.[27]

The aetiology of micro- as well macro- vascular complications among diabetes is same. Through a variety of metabolic as well as structural abnormalities performs a significant function in the onset of diabetic vascular problems.[27]

INFLAMMATION

An important part of the pathogenesis of DR is inflammation. Numerous instances of chronic inflammatory natureis reported among patients and diabetic animal models at various stages of DR. It has been acknowledged that leukostasis is a crucial pathwayamong early stages. Occlusive reaction occurring in retinal microvasculature among STZ-induced diabetic rats described first by Schröder et al. in 1991. Increased leukocyte adhesion was found in the retinal vasculature of the diabetes induced rats within three days.

Leukostasis occurring among diabetic subjects has been linked to leukocyte-endothelium adhesion, which is mediated by adhesion molecules. In experimental rats induced with diabetes and people, increased adhesive properties of leukocyte and upregulation of the b2-

integrins along with specific CD expressions have been recorded. Additionally, it has been discovered that both diabetic patients and animals have higher levels of adhesive molecules of endothelial cell like ICAM-1, VCAM-1), and selectins. The level of VCAM-1 along with values of E-selectin among patients' plasma is related to how severe their DR is. Leukocyte adhesion significantly declined among subjectshaving genetic deficiencies of CD18.

It has also been demonstrated that chemokines, perform a strong character in the pathogenetic pathway of DR. There are reports of elevated levels of chemokines among subjects with DM. In diabetic mice, MCP-1 deficiency reduces retinal vascular leakage. Additionally, diabetic patients had significantly enhanced inflammatory cytokines and their enhanced values e were correlated with severity of DR. [28- 30]

RETINAL NEURODEGENERATION

The progression of DR begins with retinal neurodegeneration. As soon as one month after the onset of diabetes, diabetic rats show signs of retinal neuron apoptosis. Among animal subjects with induced diabetes, proapoptotic variablesare significantly reported to be upregulated. Retinal degeneration in DR has been linked to mitochondrial dysfunction. High glucose exposure was shown to be linked to enhanced mitochondrial fragmentation in vitro studies. There has been extensive research on the character defined by oxidative stress among subjects with diabetes in which retinal degeneration induced. Reactive oxygen species (ROS) production is markedly enhanced in retina of the diabetic rat. Effectively preventing production of reactive oxygen species prevented visual impairment.[28- 30]

DIABETIC RETINOPATHY CLASSIFICATION[31]

Early Treatment Diabetic Retinopathy Study (ETDRS) Classification
Non-proliferative Diabetic Retinopathy
• **No retinopathy**: No retinal lesions
• **Very mild NPDR**: Microaneurysms only
• **Mild NPDR**: A few microaneurysms, retinal haemorrhages & hard exudates
• **Moderate NPDR**: Retinal haemorrhages (about 20 medium-large per quadrant) in 1-3 quadrant + cotton wool spots (between the grades mild and severe NPDR)
• **Severe NPDR:** fulfilling one rule of the 4-2-1 rule.
o **4-2-1 rule**
▪ Severe haemorrhages in all four quadrants
▪ Venous beading in 2 or more quadrants
▪ Moderate IRMA in 1 or more quadrants
• **Very Severe NPDR:** fulfilling two or more rules of the 4-2-1 rule.
Proliferative Diabetic Retinopathy
• **Mild to moderate PDR**- NVD or NVE insufficient to meet high-risk characteristics
• **High-risk PDR**-
o NVD greater than ETDRS standard photograph 10A (about 1/3 disc area).
o Any NVD with vitreous haemorrhage.
o NVE greater than 1/2 disc area with vitreous haemorrhage.

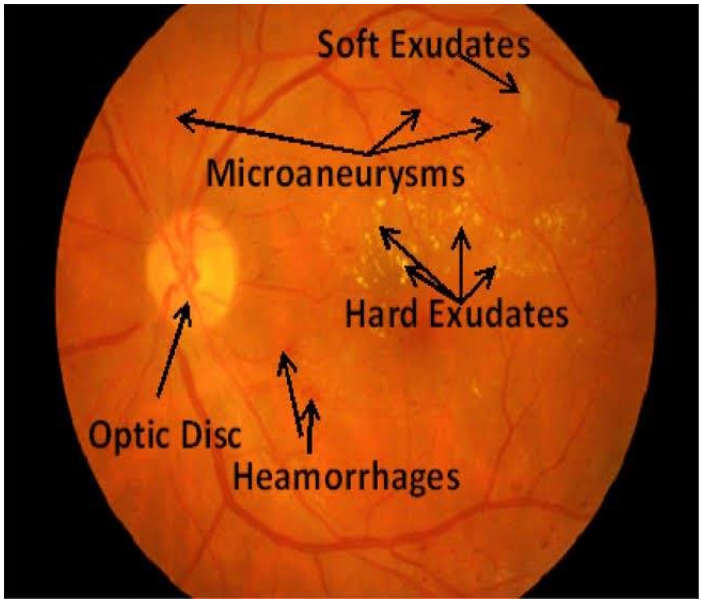


Figure 8: Signs of DR

Figure 9: Fundus picture of PDR

Advanced Diabetic Eye Disease

It is a DR's devasting adverse event among subjects especially in which therapeutic protocol was unsuccessful.

Figure 10: Fundus picture ofAdvanced Diabetic Eye Disease

MACULAR THICKNESS

Upper range of macular thickness in healthy eyes, as reported by Chan A et al was 250 µm while data from western countries have reported the mean macular thickness ranging between 133 µm to 182 µm. Indian studies have reported a mean macular thickness; extending upto was 287.87 µm (Natung T et al). Among paediatric subjects (between 5 to 17 years), mean macular thickness is reported to be 114.88 µm. Conventional evaluation of macular edema by employing using procedures like fundus photography, fluorescein angiography etc done exhibit any sensitivity to minute alteration in thickness. OCT isemployed for quantitative

evaluation of thickness of retina. Being non-invasive, it is a better modality in comparison to others.[14, 32]

Diabetic Macular Edema (DME) can be classified into the following groups

- Focal exudative and diffuse maculopathy
- Ischemic and non-ischemic maculopathy
- Tractional and non-tractional maculopathy
- Centre involving macular edema and non-centre involving macular edema

ETDRS Definition of Clinically Significant Macular Edema (CSME)

- Retinal edema within 500 μm of the center of the fovea
- Hard exudates within 500 μm of the center of the fovea if associated with adjacent retinal thickening (which may be outside the 500 μm limit)
- Retinal edema one disc area (1500 μm) or larger, any part of which is within one disc diameter of the center of the fovea

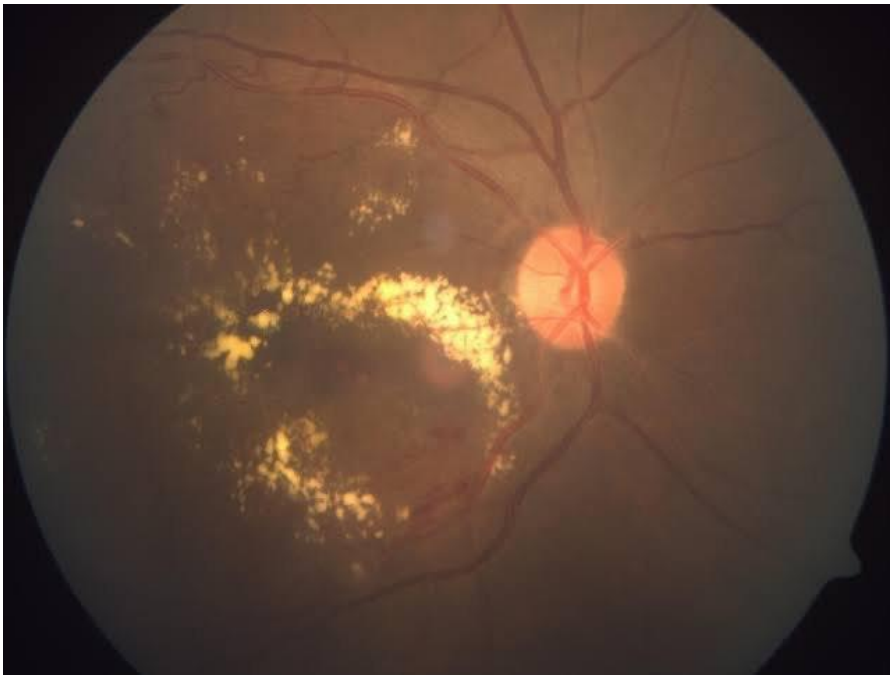


Figure 11: Clinically Significant Macular Edema

OCT (optical coherence tomography) Classification of Diabetic Macular Edema

- Sponge-like thickening of retinal layers
- Large cystoid spaces
- Serous detachment of the retina
- Tractional detachment of the fovea or vitreomacular traction
- Taut posterior hyaloid membrane.

International Clinical Diabetic Retinopathy Disease Severity Scale

- ***No apparent retinopathy***-No abnormality
- ***Mild NPDR***- Microaneurysms only
- ***Moderate NPDR*** -More than just microaneurysms and less than severe disease
- ***Severe NPDR*** -No signs of PDR and any of the following:
    - 20 intraretinal hemorrhages in each of the four quadrants
    - Venous beading in ≥2 quadrants
    - Prominent IRMA ≥1 quadrant
- ***PDR*** - One or more of the following:
    - Neovascularization
    - Vitreous or pre-retinal hemorrhage

In relation to DME:

- '**DME apparently absent**'- Apparent retinal thickening and hard exudates at the posterior pole are absent.
- '**DME apparently present**'- There is some 'apparent retinal thickening and hard exudates at the posterior pole.' It can further be classified into mild, moderate, and severe based on the distance of thickening and hard exudates from the center of the fovea.
    - ***Mild DME***: The retinal thickening or hard exudates are located far from the center of the fovea.
    - ***Moderate DME***: Retinal thickening or hard exudates are approaching the center of the macula but not involving the center

Severe DME: Hard exudate and thickening involve the center of the fovea.

OPTICAL COHERENCE TOMOGRAPHY (OCT)

Over the past 20 years, OCT has become increasingly crucial for ocular disease diagnosis. The non-invasive in vivo analysis of retinal tissue using OCTis a crucial tool for diagnosis and treatment involving glaucoma and various retinal diseases.[32]

With development of OCT, the macula could be imaged cross-sectionally or tomographically with micrometre resolution for medical diagnostic purposes. OCT uses a similar mechanism to ultrasound B-mode imaging. Use of OCT in the diagnosis of a number of macular disorders, such as CSME, macular holes, and choroidal neovascular membrane, is well-established.[33]

Utilities of OCT involves detection and quantitative evaluation of DME and retinal thickness, which are related to changes in reflectivity in the retinal layers that are more pronounced and to low reflectivity in the external retinal layers.[33]

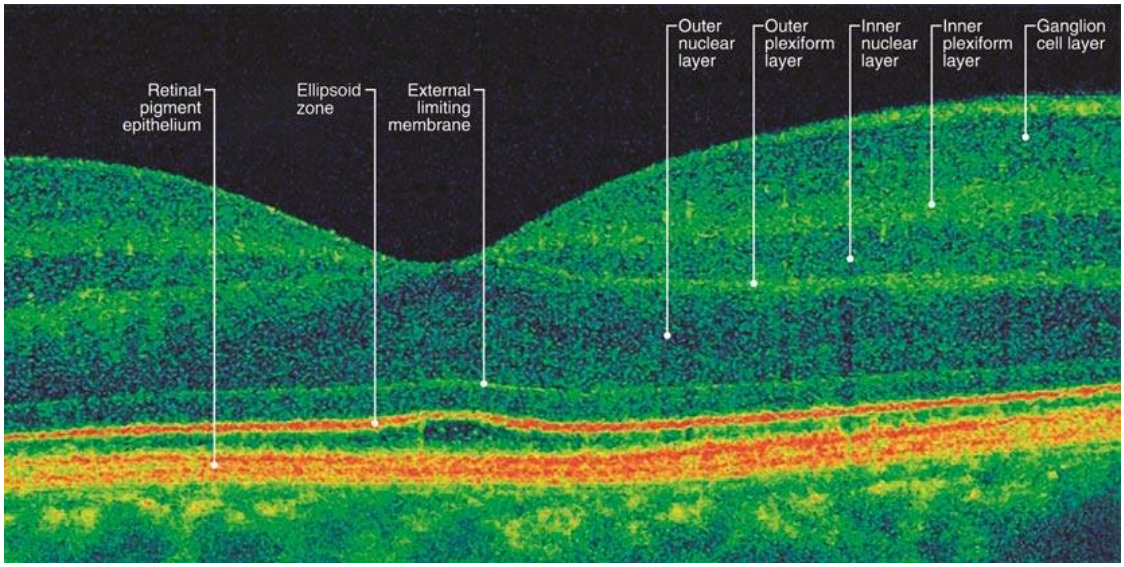


Figure 12: Normal OCT picture with Retinal layers

Principles of OCT

It is not possible to evaluateminute details inside eyeball with any external measurement system since light travels at a high speed ($3*10^8$ m/s). However, because of the wave-like nature of light, it is possible to time how long it takes to travel a specific distance. Coherence length refers to the length light will have to move while in process of coherence time, &coherency refers to evaluation of what 1light's wave is associated with another. With the help of interference for detection of phase differences among waves of light,visuals with micron-scale near of tenacity could be created by linkingtime of flight of sample reflection's to known delay of reference reflection. This serves as the foundation for TD-OCT, which samples a miniature area at single time point. Because a longer time period is required to obtain a pictureof whole posterior pole, TD OCT is ineffective. [34]

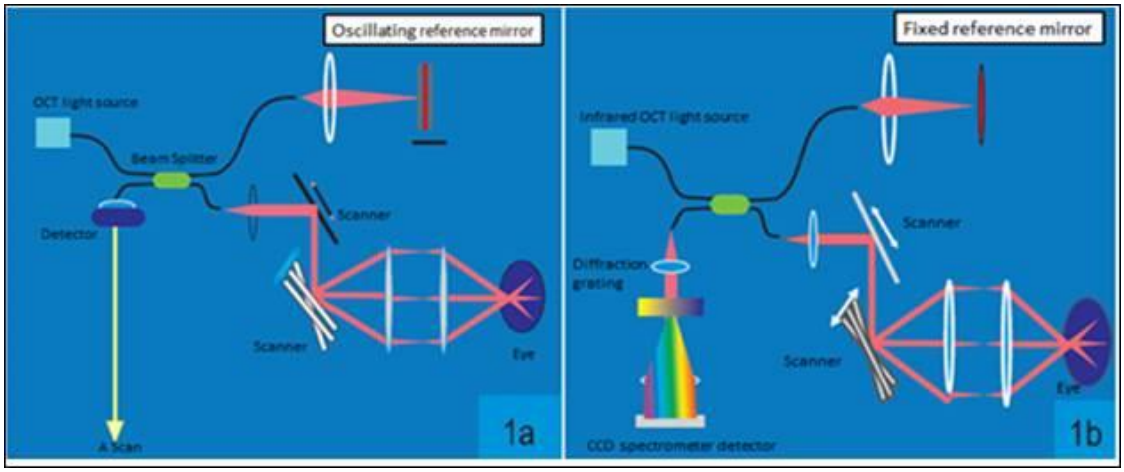


Figure 13: Principle of OCT

The second generation of OCT, known as spectral domain (SD) OCT, uses a grating to separate the individual wavelengths of light coming from an interferometer. Simultaneously assessment of nature of various reflections among sample arm is possible by employing a Fourier transform. In order to extract images of whole tissue, SD-OCT is significantly greater effective (far more than TD-OCT). [34]

Deeper structures like the choroid can be seen when the inner sclera, where SD OCT's peak sensitivity is located, is placed posteriorly. By placing choroid-scleral interface close to the zero delay, enhanced depth imaging (EDI) with SD OCT can now offer a non-invasive way

to increase visualisation of the choroidal anatomy. By choosing the EDI function in the software, it can be done with SD OCT instruments that are commercially available.[34]

Figure 14: OCT Machine

Being a non-invasive technique, OCT produces depth-resolved visuals using low-coherence interferometry. Interferometrical dimensions are attained by intrusiveaction with reflectance or even backscatter from ophthalmiccomponents while a light beam is employed to analyse a region of the ocular portion. When using OCT, this alteration of conventional Michelson interferometry enables creation of morphological visuals of anatomic structures. Since its introduction in 1991, OCT has been in extending use; especially in the ocular assessment.[35]

OCT INDICATIONS

Indications

In-situ and real-time quantitative as well as qualitative evaluation of examined tissues are both provided by OCT.

It can also detect fluid beneath retina or in the retinal layers, which may not be visible clinically. It can also detect macular holes, pseudoholes, epiretinal membranes, vitreo-macular adhesion, vitreo-macular traction, retinoschisis, retinal detachment, diabetic retinopathy, age-related macular degeneration, retinal nerve fibre layer thickness, optic disc parameters, and asses posterior segment lesions. OCT cannot and should not be used to diagnose any ocular disease on its own. Additionally, no ocular pathology should ever be diagnosed or treated solely based on this standard.

In addition to the pertinentpast of the pathologic process, the Doctor should possess different remainingdata available, like reliable perceptions of patients' ophthalmic pathologies, FA,ICGA, bio microscopy, and more.[35]

OCULAR APPLICATIONS OF OCT

These include intraretinal collections &subretinal collections

Intraretinal fluid collections include upcoming macular holes, cysts, microcysts, and retinal edema (focal or diffuse). OCT offers sequential scans that are useful for estimating the volume of subretinal and/or intraretinal fluid.

Retinal Edema- Edema is the main factor contributing to retinal thickening. Monitoring surgical or non-surgical intervention and assessing the pathologic process' progression are two of OCT's major accomplishments. The following manifestations of retinal oedema may occur singly or together:

Focal or Diffuse Eddma- At first, there might not be any changes at all. OCT may reveal increased retinal thickness and decreased reflectivity. OCT scans show a spongy feature in retina that is noticeably edematous.

Cystoid macular edema (CME)- In clearly defined retinal spaces, there is intraretinal fluid accumulation (outer plexiform layer). The anatomical configuration of the outer plexiform layer and the vertical Müller fibres are responsible for the rosette- or petalloid-like appearance. Diabetes, ARMD, venous occlusions, pars planitis, uveitis, pseudophakia, Irvine-Gass syndrome, and retinitis pigmentosa are common causes of CME. The central macula's outer nuclear layer exhibits diffuse cystic spaces as well as increased retinal thickness, which is maximally concentrically measured as central subfield thickness in OCT printouts.

Serous retinal detachment- occurs after long-term oedema. Between the retinal pigment epithelium (RPE) and the sensory retina, or within the retinal layers, the cysts lose their septae and combine to form one or more fluid-filled pools.[35]

Subretinal fluid collections

OCT is also used to diagnose conditions like retinal pigment epithelial detachment, disciform scars and subretinal fibrosis, epiretinal membranes (ERM)/Macular pucker (cellophane maculopathy), vitreomacular traction, rhegmatogenous retinal detachment, macular pseudoholes, lamellar holes, full thickness holes, retinoschisis, age-related macular degeneration.[35]

OCT CHANGES IN DIABETIC RETINOPATHY

Since 2002, OCT has significantly advanced knowledge of diabetic retinopathy. It has completely changed how DR is assessed and how it will likely progress.Diabetes-related macular oedema and non-proliferative diabetic retinopathy (NPDR) (DME).

On OCT, thinning of retina might occur under the effect of ischemia. Appropriate use clinical evaluation along with FA might be helpful in directing the pathway of treatment in DR. A significant correlation in macular edema, which is unresponsive for laser therapy is macular traction. Such eyes exhibit diffuse leakage on FA and have taut posterior hyaloid. The findings of flat foveal contour, thickened, hyperreflective vitreoretinal surface, and diffuse cystic retinal thickening on OCT are all very helpful in diagnosing this condition. 12 The following analysis in DR is made possible by OCT, which also aids in determining the etiologic profile of visual impairment: the site and degree of retinal oedemanot only overall, nut also inside various retinal layers.[35- 38]

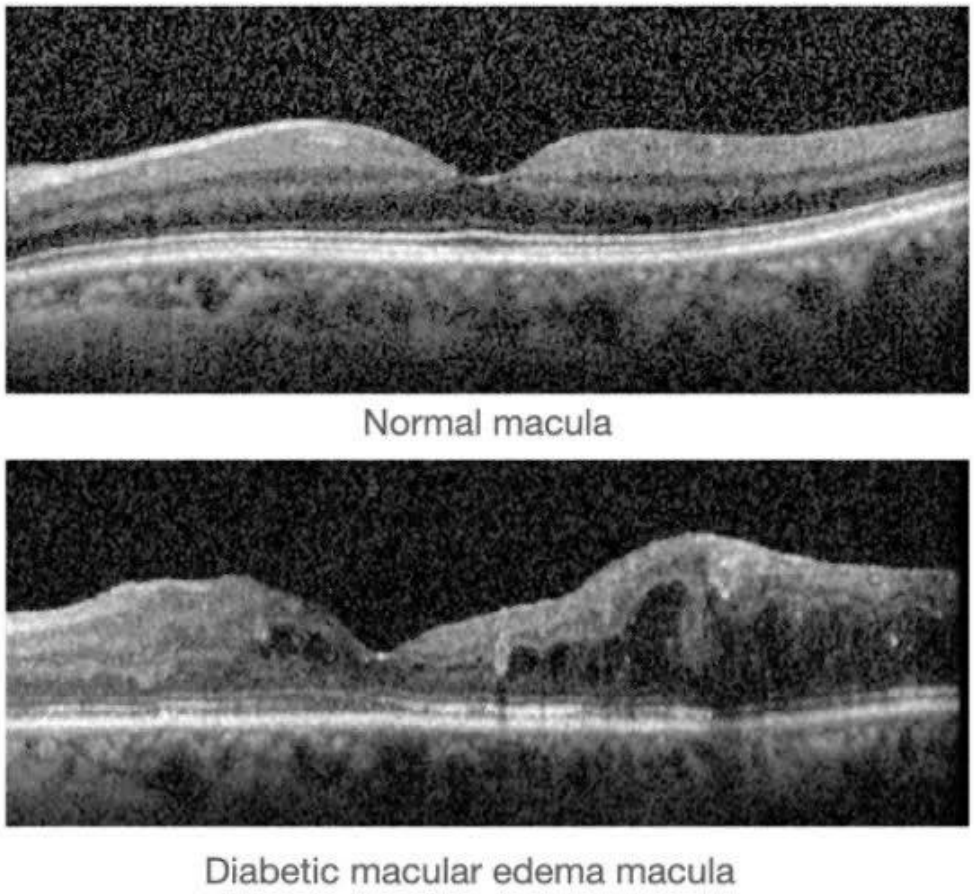


Figure 15: OCT image of DME

• Indications and extent of photocoagulation therapy
• Assessing the success of surgical, intravitreal, or laser treatment.
• Common pathophysiologic lesions in DR Cotton-wool spots show up on OCT as elongated, hyperreflective nodules in the nerve fibre layer, frequently casting a shadow on the posterior layers.
• In deeper retinal layers, hard exudates can be seen as hyperreflective formations. DR, hypertensive retinopathy, Coats disease, telangiectasias, and radiation retinopathy are common causes.
• Hyperreflective scans of the posterior layers with retinal haemorrhages.
• Fibrous tissue—shows up as an area that is more reflective than usual and distorts the macular outline.[35- 38]

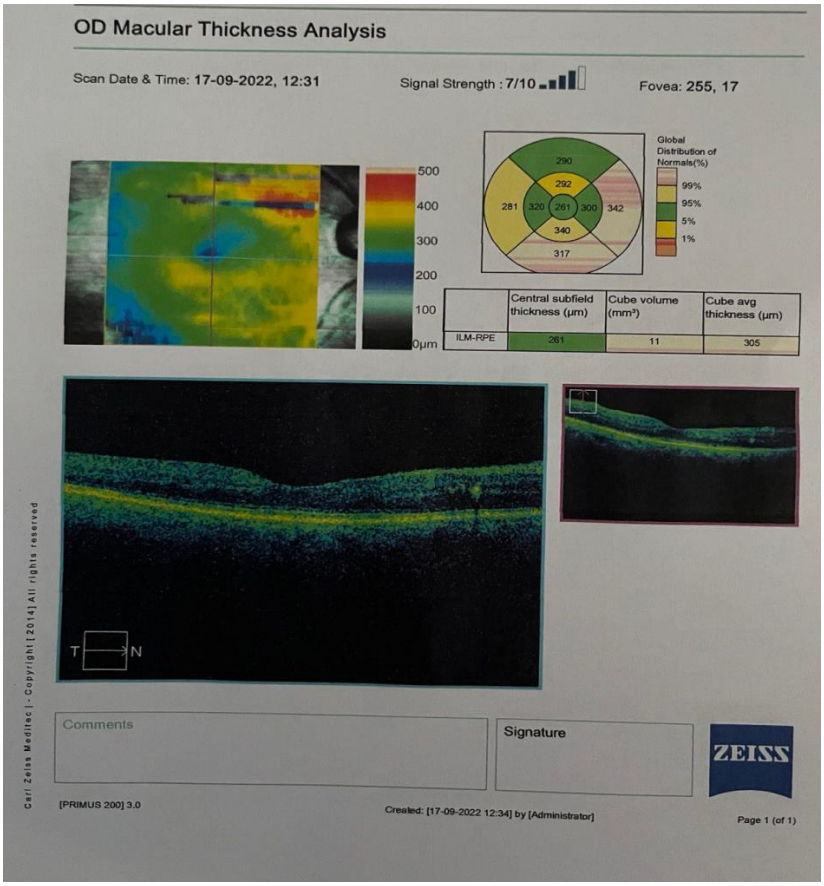


Figure 16: OCT Report

Retinal oedema is characterised by thickened, hypo reflective, and spongy retina in OCT scans. Retinal mapping is used to locate the oedema and retinal thickness and volume measurements are used to calculate its size. OCT makes it possible to localise oedema more accurately than FA can. Microcavities eventually combine and produce pseudocysts, that are clearly visible in OCT images. A completely developed DME may affect the entire retina, with the retinal tissue disappearing, the cavities coalescing, and a completely serous detachment of retina as a result. The elevated retina and RPE in such eyes are separated by an optically clear cavity, according to OCT. Monitoring the efficacy for intravitreal medications

in context to retinal thickness as well as retinal volume has been among the original ascendancy of OCT.

The most common techniques for detecting diabetic retinopathy as well as diabetic macular oedema are ophthalmoscopy, fundus photography, and fluorescein angiography. To improve the diagnosis as well as management of retinopathy, high-resolution imaging of ocular tissues is becoming more and more in demand. The retina can be imaged using optical coherence tomography (OCT), which offers valuable additional information. It generates accurate, repeatable as well as objective scans of retina, particularly when detecting diabetic macular oedema, also, it offers details on vitreoretinal associations which are obviously only detectable with OCT. It improves the precision with which vitreomacular or vitreoretinal traction, epiretinal membranes, or diabetic macular oedema are diagnosed. OCT also sheds light on the morphological alterations to the retina caused by diabetic retinopathy. This proves that macular oedema seems to be a complicated clinical condition with a range of morphologies. With OCT, structural alterations as well as quantitative assessment of this condition as adamantoid by the thickness as well as volume of retina have become possible. OCT is much more sensitive as compared to slit-lamp bio microscopy to minute variations in retinal thickness.[35, 39, 40]

- In healthy individuals as well as those having diabetes without having diabetic retinopathy, the retinal thickness was measured and evaluated by **Fritsche P et al in 2002**. On the retina, a beam had been directed and imaged over a two mm by two mm area in two hundred milliseconds. Ten healthy individuals and nine type 1 as well as type 2 diabetic patients who did not have funduscopic or photographic evidence of diabetic retinopathy were imaged using RTA. The RTA's intra- as well as inter-

individual variations were identified. The variability within and between individuals was five meters as well as fifteen meters, respectively. The average value of mean foveal thickness as well as perifoveal retinal thickness within a group of ten healthy subjects was 152.15 meters as well as 175. 14 meters, accordingly, whereas in a cohort of 9 diabetics not having symptoms of retinopathy, it was 181. 26 meters as well as 191. 27 meters, correspondingly. Diabetes patients' MFT was considerably greater as compared to control cohorts. As compared to the outcomes in healthy participants, retinal thickness was higher in patients having diabetes without diabetic retinopathy in all measurements.[41]

- Using optical coherence tomography (OCT), **Sugimoto M et al. (2005)** found initial diabetic damage among T2DM subjects without diabetic retinopathy and evaluated OCT as a clinical test. 32 patients (n = 32) with NDR were enrolled. OCT was employed to estimate the width of the retina and the retinal nerve fibre layer. For the measurements of retinal thickness as well as RNFL thickness, 2 healthy communities were also enrolled. To assess the predictor variables, the ROC curve had been created. In the superior regions, RNFL width noticeably decreased as well as retinal width considerably increased when comparing the normal and NDR eyes. For superior retinal width as well as superior RNFL thickness, respectively, the area below ROC curve was 0.65 and 0.63. [42]

- In patients with diabetic retinopathy, **OZdek SC et al. 2005** compared optical coherence tomography characteristics to clinical as well as fluorescein angiographic outcomes. In a retrospective study, one hundred and ninety five eyes of one hundred and ten subjects with several phases of retinopathy as well as forty eyes of twenty

controls underwent an ophthalmologic examination along with FA and OCT images. The OCT images showed serous foveal detachment along with inflammation in over six percent of the eyes, serous foveal detachment along with inflammation and CME in over three and a half percent of the eyes, regular foveal morphology in over twelve percent of eyes, and retinal inflammation in sixty six percent of eyes. The central foveal thickness was strongly linked to the best-corrected visual sensitivity. The clinical examination and OCT results were 77% in agreement. 15.4% of the study's eyes had CME detected with OCT, compared to 40% who had it missed by slit-lamp bio microscopy and 63.3% who had it undetectable by FA. These findings show that OCT can help diabetic patients and their carers decide on a treatment plan (surgical or medical), that is important in the initial phases of diabetic maculopathy if the structural modifications are invisible with slit-lamp bio microscopy or angiographically. [43]

- **Chou TH et al. 2009** examined the association among central foveal width as determined by OCT in diabetic patients and glycosylated haemoglobin (HbA1c). In this cross-sectional study, 102 patients' eyes totalling 102 were examined. The CSME detected by OCT in diabetic patients was not numerically associated to gender, right eye or the left eye, DM period more than ten years or necessarily not as well as AC sugar content, according to a univariate analysis (over 140 or not). OCT results revealed a strong as well as favourable correlation between macular width as well as HbA1C value as well as and age. Age or=50 and HbA1c >or=8% were found to be risk factors with a tendency to increase. Macular thickness increased in T2DM subjects having HbA1c of 8 or higher, as well as there existed a statistically strong relationship among young age, short DM period as well as broader macular width. [44]

- In diabetics without diabetic macular oedema, **Yeung L et al. (2010)** looked at the relationship among HbA1c content as well as macular volume. They conducted a cross-sectional observational study. Subjects having DM without DMO for over ten years were included. Each patient's single eye was chosen for analysis. Proliferative diabetic retinopathy-affected eyes were not included. Optical coherence tomography was used to measure the central subfield thickness, central subfield volume and total macular volume. The average HbA1c level from the year before recruitment was used to define chronic HbA1c levels. In those having diabetes lasting longer than ten years without having DMO, the HbA1c value favourably associates with macular width as well as volume. According to the findings, DMO may manifest clinically before subclinical changes in macular volume and thickness have taken place. Early, strict glycaemic control before the onset of DMO may be crucial in preventing the decline in macular function by changing the haemodynamic of the macula. [45]

- Glycated haemoglobin (HbA1c) levels were compared in subjects having diabetic cystoid macular oedema with as well as without serous macular detachment in **Turgut B et al's 2010** study (SMD). The study included thirty subjects having diabetic CME in each eye but no SMD as well as thirty subjects having diabetic CME as well as SMD in each eye, as determined by OCT as well as fundus fluorescein angiography. HbA1c levels were estimated using high performance liquid chromatography in additament to measurements of central macular width by OCT as well as visual acuity via initial management NDR study chart. The test got utilised for the purpose of statistical analysis on independent samples. In subjects having diabetic

CME, the evidence of SMD and high HbA1c levels may be an indirect indicator of retinal pigment epithelium dysfunction. [46]

- **Moon SW et al. (2011)** used optical coherence tomography to demonstrate the change in macular thickness in diabetic subjects as well as to evaluate its association to HbA1c concentrations. Those with diabetes who recieved at minimum 2 OCT measurements of macular width over the course of a year were included. Clinical information including age, insulin therapy, systemic hypertension as well as the degree of retinopathy were gathered, as well as HbA1c readings within one month of each OCT study. Three macula parameters, including total macular volume (TMV), central sub foveal macular thickness (CSMT), and centre point thickness (CPT), were changed between two measurements. Based on ½ width of ninety five percent of confidence interval for percent modification, subjects were split in 2 cohorts: the increase cohort as well as the decrease cohort. Correlation analysis and group comparison were used to examine the relationships between CPT variation, CSMT variation as well as TMV variation and reference HbA1c concentrations, HbA1c variation as well as other clinical variables. Over a period of less than a year, the macular width as well as volume changed according to HbA1c values. Possibility for the increase in macular thickness included an increased baseline HbA1c as well as a significant decline in HbA1c.[47]

- In order to evaluate any potential increased macular width linked to DM, **Demir M et al. (2013)** contrasted CMT of diabetic subjects to T2DM in the absence of clinical retinopathy as well as normal controls. Measurements of OCT were made in 120 eyes

of 60 healthy patients (control group) and one hundred and twenty-four eyes of sixty two patients having DM who did not have clinically evident retinopathy. In each case, blood biochemistry parameters were examined. The amounts of fasting plasma sugar as well as glycosylated haemoglobin, as well as central macular width data, were compared between these two groups. Subjects having T2DM who didn't show clinical retinopathy had central macular thickness that was not statistically different from that of healthy subjects. [48]

- In a rural South Indian community, the occurrence rate of T2DM and diabetic retinopathy was estimated by **Raman R et al in 2014**. The method employed was multistage cluster sampling. Each eligible participant had a thorough eye exam. All subjects got their fundi scanned using 45°, 4-field stereoscopic digital photography, and patients with NDR also had their fundi photographed using 30°, seven-field stereoscopic digital pairs. Based on Klein's classification, diabetic retinopathy was identified. In rural Indians, the prevalence of diabetes was 10.4%, and among those who had diabetes mellitus, the prevalence of diabetic retinopathy was 10.3%. On a multivariate analysis, the following factors were statistically significant and linked to a higher risk of diabetic retinopathy: gender, insulin use, longer duration of diabetes, systolic hypertension, and participants with poor glycaemic control. Over the age of 40, almost 1 in 10 people in rural South India exhibited signs of type 2 diabetes mellitus.[49]

- In patients with diabetic retinopathy in the early stages, **Oshitari T et al. (2014)** looked at a strong association among Fourier-domain optical coherence tomography criteria as well as the level of HbA1c and period of DM. The Chiba University Hospital examined 30 patients with early-stage DR, and 30 of their eyes were examined. By using FD-OCT, it was possible to measure the width of ganglion cell unit, the retinal nerve fibre layer as well as the macular map 5 (MM5). By using Spearman rank correlation, the coefficients of association among these criteria as well as the HbA1c value along with the length of disease were calculated. Significant correlations were found between the HbA1c level and the width of bottom sector of the MM5's outer ring. Significant correlations between the DM duration and the outer ring's superior and temporal sectors were found. The results suggested that a subclinical rise of vascular permeability might be the reason for the strong favorable association among the retinal width of sectors in the exterior ring as well as the HbA1c content along with period of DM. The fact that Müller cell density is said to be increased in the perifoveal region as compared to the central region may have also played a role in the correlation.[50]

- Changes in choroidal as well as retinal width in people having T1DM were investigated by **Yolcu U et al. in 2016**. (DM). In their prospective case-control clinical study, 60 subjects having Type 1 diabetes as well as sixty age as well as gender-matched healthy subjects were enrolled. A thorough ophthalmological investigation was carried out on all patients. Spectral-domain OCT was used to measure each participant's ChT at fovea as well as the horizontal nasal & temporal quadrants at five hundred-m intervals to one thousand five hundred-m from the foveola. Age, gender, the length of the disease, the level of fasting sugar, axial length

as well as refractive errors were recorded and analysed. In diabetic patients, the average HbA1c was 8.9 percent, average fasting blood glucose was 287.5 mg/dl, and average disease duration was 6.1 years. The patients' and subjects' differences in age, gender, AL, and spherical equivalent were not statistically significant ($p>0.05$). Diabetes patients had significantly lower sub foveal ChT, nasal quadrant ChT estimations, temporal one thousand five hundred meters as well as average nasal ChT. Temporal five hundred-m as well as one thousand-m ChT estimations, average ChT, central and mean macular thicknesses, and ChT did not significantly differ between the groups. [51]

- A 16-month, randomised, prospective, interventional study was carried out by **Kumar J et al in 2017** in sixty eyes of thirty diabetic subjects who had macular oedema. The eyes got categorised into 2 cohorts: Group A, that comprised thirty eyes from fifteen subjects, and Group B, that comprised thirty eyes from fifteen subjects. Average HbA1c value as well as average central macular width were distinct from reference to three months, six months as well as nine months follow up. In group A, the average reference serum HbA1c amounts were 7.91 whereas in the second cohort, they were 11.42. At three months of recall, group A's average reference HbA1c amount was 7.56, while group B's was 10.32. At 6 months, group A has a score of 7.26 while group B has a score of 9.44. Group A has a score of 6.78 at 9 months, while group B has a score of 8.32. In group A, the mean baseline central macular thickness was 688.13 microns and in group B, the mean CMT is 681.33 microns. After At three months, group A's mean central macular thickness was 446.73 while group B's CMT was 568.86. Group A's CMT is 375.93 after six months, while group B's CMT is 486.66. Following a 9-month follow-up, group A's CMT is 289.00 while group B's

CMT is 376.60. The notable decline in the mean serum/HbA1c level also demonstrates the decline in the mean CMT.[52]

- In research conducted by **Peng YJ et al** in 2108, authors assessed impact of metabolic profile on CMT using OCT among DR subjects with and without CME. In patients without macular oedema, higher HbA1c levels showed significant inverse correlation with CMT. They concluded that in diabetic patients with coexisting macular oedema, accurate metabolic statusmight not be correlate to improvedCMT.[53]

- The CMTof subjects with presence of type 2 DM and absence of DR was compared with healthy controls in a study conducted by **Murugesan S et al. in 2018.** 170 patients participated in this study (85 cases and 85 controls). From the time of diagnosis to 15 years, diabetes could be present. Mean CMT was 198.47 m among subjects with DM type 2 and 235.68 m in healthy control group. Men with diabetes had thicker CMT than women with diabetes (P = 0.00). No significant correlation of diabetes duration/glycaemic profile was seen with CMT. Compared to healthy controls, diabetic subjects had a thinner CMT.[54]

- **Sami I et al. (2018)** compared optical coherence tomography (OCT) and fundus photography results for diabetic mellitus (DM) patients' macular changes (FP). At a tertiary care facility, this prospective comparative study was carried out. 200 diabetic patients' eyes were examined using slit-lamp bio microscopy, colour FP with a TOPCON fundus camera, and cirrus OCT. Haemoglobin A1c (HbA1c), postprandial

blood sugar (PPBS), and fasting blood sugar (FBS) were all measured.In comparison to patients with normal OCT (5.52 2.18), patients with OCT changes had a higher mean HbA1c (7.08% 2.9%). On OCT, presence of retinopathy was seen among 55 eyes (27.5%) & in 74 eyes (37%) on FP. 75 eyes (59.52%) of the 126 eyes with normal fundus had OCT changes. The average macular thicknesses in the central fovea, parafovea, and perifovea were 260.95 65.16, 322.78 47.96, and 281.73 36.77 m, respectively, in an OCT. Increased foveal and peripheral (parafoveal and perifoveal) thicknesses were present in the retinopathy-affected eyes. In 59.2% of the eyes, the OCT revealed changes without clinical retinopathy, indicating a potential role in the identification of subclinical retinopathy. However, the fovea in the eyes with clinical retinopathy was thicker, suggesting a more serious disease and retinopathy.The likelihood of OCT changes increased with higher HbA1c values. [55]

- Diabetic subjects who did not exhibit any clinical symptoms of diabetic retinopathy had their early changes in retinal thickness along with OCTA variables assessed by **Vujosevic S et al in 2019.**Evaluation of 90 subjects' eyes (twenty-four, thirty-sex and thirty subjects were of type 1 diabetic status, type 2 diabetic status and healthy contorls. The inner retinal layer and perifoveal capillary loss in the SCP are closely related. These data might aid in classifying patients with diabetic retinopathy who are still in the preclinical stages of the disease. [56]

- Using optical coherence tomography, **Sethia R et al. 2019** investigated the relationship between HbA1c and macular thickness (OCT). Fifty eyes among subjects

with confirmed diagnosis of diabetes (Type 2) were enrolled. Only those diabetic subjects were enrolled in which mild to moderate NPDR was present. Division of the subjects was done into three study groups after they underwent phacoemulsification surgery; Group 1, Group 2 and Group 3 comprised of subjects with HbA1c values less than 6.5%, 6.5 to 8% and more than 8%. Their research didn't observe any significant correlation of central foveal thickness with HbA1c values. Also, no nearby correlation of HbA1c with alteration in visual acuity was seen. They reported presence of significant enhancement of central foveal thickness (CFT) at thirty-day follow-up postoperatively; which was independent of HbA1c levels. BCVA and CFT wereunaffected by HbA1c. After phacoemulsification, diabetics exhibit a change in central foveal thickness, though this isn't always related to poorly controlled diabetes. [57]

- CRP and glycosylated haemoglobin (HbA1c) were found to be correlated with the severity of DME by **Gopinath G et al in 2019**. 75 type 2 diabetic cases with confirmed presence of DME and another set of seventy-five subjects with presence of diabetes but absence of DME were enrolled.On the basis of severity of CMT, division of the subjects of study group was done into subjects with mild, moderate and severe macular edema. CRP levels were elevated in 32 cases and five controls. They also reported presence of significant association among CRP levels with DME's severity. Increased severity of DME was linked to elevated HbA1c levels. In light of significant character that inflammation plays for occurrence of DME, CRP levels as well as HbA1c levels can be used as biomarkers to assess the severity of DME. [58]

- **Tadwalkar A et al. 2019** used OCT to compare CMT among control subjects and diabetic subjects without DR. identification and treatment of DR was improved by early and adequate identification by OCT by virtue of its property of creating accurate along with and objective images of the retina (especially among patients with DME). It improves the precision with which vitreomacular or vitreoretinal traction, epiretinal membranes, or diabetic macular oedema are diagnosed. In diabetic retinopathy, OCT aids for identifying clinical alterations of retinal component. It proves that CME, a complex clinical entity with a variety of morphologies, exists. [59]

- Spectral domain optical coherence tomography was used by **TorabiH et al. in 2019** to evaluate the cocreation among HbA1c levels and choroidal thickness amongdiabetic individuals. One hundred and eighty eyes among ninety diabetic subjects were evaluated. Division of all the subjects was done among 3 groups as follows: Group 1- Subjects with adequate glycaemic control, Group 2- Subjects with glycaemic control of moderate level while group 3 included subjects having poor glycaemic control. Healthy controls which were age and gender matched were placed in group 4. Among subjects with presence of diabetes mellitus, choroidal thickness and HbA1c values showed significant correlation. They concluded that improving the status of body's glycaemic profile might lead to prevention of choroidal thinning. [60]

- In subjects with DM, **Mikhail ME et al 2021** found a correlation between RNFL and GCC and glycosylated haemoglobin (HbA1c). In group 1, where HbA1c levels were

greater than 9%, there existed significant association (negative) of HbA1c with RNFL. Additionally, in group 1, there was an association amongvolume of focal loss with glycaemic status. Among subjects with HbA1c values less than 9 percent, significant association among glycaemic status with average/inferior GCC thickness was seen. Furthermore, HbA1c had poor association among both volume of focal loss and volume of global loss. [61]

- In patients with non-proliferative diabetic retinopathy, **Muhammad Badr Salah El-Deen A et al** 2021 examined the relationship between macular thickness and glycosylated haemoglobin. One hundred subjects with type 2 diabetes were enrolled; with 100 eyes each. One group of diabetic patients had no diabetic retinopathy, and the other group had non-proliferative diabetic retinopathy. Together, 100 eyes were divided into two equal groups. The difference between the groups of people without diabetic retinopathy and those without it was statistically insignificant, but the group without it had a shorter duration of the disease, a lower HbA1c level, and lower total macular volume (TMV) than the NPDR Group.The findings demonstrated that in both the no DR and NPDR groups, central subfield macular thickness (CST) is positively and significantly correlated with glycosylated haemoglobin (HbA1c) level, and that the severity of the DR stage was significantly correlated with higher HbA1c levels. Additionally, the findings demonstrated a strong correlation between macular thickness and DR stage severity across all nine of the common ETDRS subfields. There was significant association among the diabetes duration and HbA1c levels.A notable inverse relationship between insulin use and HbA1c level and a significant inverse relationship between insulin use and the prevalence of DR was also observed om results. Increased levels of glycosylated haemoglobin in type II diabetic patients

were linked to increased incidence of DR, increased macular thickness, and increased incidence of diabetic macular oedema. [62]

- **Bernal-Morales C et al in 2021** assessed one hundred fifteen controls and four hundred seventy-eight type 1 DM patient. Controls, patients without DR, patients with DR were evaluated followed by subgroup analysis on the basis of HbA1c levels.Age and gender-based analysis showed significant among different study groups in terms of both VD and FAZc. There existed a significant association among HbA1c and CRT in subjects with DR and having levels of HbA1c less than seven and a half percent. Higher HbA1c valueswere linked to structural OCT alterations among subjects with DR and OCTA alterations among diabetic subjects without DR.[63]

- The average CMT among diabetic subjects along with prevalence of abnormal CMT was valuated in a previous study conducted by **Kagmeni G et al in 2022**. Average age was approximately fifty-seven years with mean CMT being 229.6 53.8 m on average. Optic coherence tomography, as opposed to fundoscopy, identified retinal abnormality among seventy eight percent of the subjects. Peri foveolarinspissation, macular thinning, along with occurrence of macular oedema were the prominent abnormalities identified. In their population, optical coherence tomography has made it possible to identify subclinical macular oedema early on. [64]

- The CCT and CMT of diabetic subjects were compared with controls in a study conducted by **KAZANCI B et al in 2022.** A comparison was made between forty-seven controls and 50 diabetic subjects. Less than eight percent of HbA1c levels was found among diabetic subjects. Diabetes patients' VA logarithms was lower in comparison to controls.CCT and CMT values, however, were similar among diabetic and non-diabetic subjects. Diabetic subjects which did not have DR in the study did not differ from non-diabetic controls at CCT or CMT. [65]

MATERIALS AND METHODS

MATERIALS AND METHODS

SOURCE OF DATA:

Patients visiting Ophthalmology outpatient department at R.L. JALAPPA HOSPITAL AND RESEARCH CENTRE,TAMAKA, KOLAR attached to SRI DEVARAJ URS MEDICAL COLLEGE for routine check-up or refraction.

STUDY DURATION: 21 Months (January 2021 and September 2022)

SAMPLE SIZE: 162 eyes (81 Patients)

STUDY DESIGN: Cross sectional comparative study

INCLUSION CRITERIA:

1. Patients with Type 2 Diabetes Mellitus

2. Duration of Type 2 Diabetes Mellitus greater than / equal to 10 years

3. Patients presenting directly to Ophthalmology OPD and those referred for ophthalmic evaluation from other specialities.

4. Patients recently diagnosed as Diabetic macular edema, without any treatment / intervention.

EXCLUSION CRITERIA:

1. Prior Intraocular surgery, focal or Pan retinal Photocoagulation and periocular or intravitreal injection of any medication,
2. History of Agerelated macular degeneration, macular hole, central serous retinopathy, any other macular pathology,
3. Patients on oral Glitazone, topical Latanoprost, pilocarpine.
4. Opacity of ocular media (cornea, lens, vitreous) if significant enough to interfere with OCT examination
5. Uncontrolled systemic hypertension, Hyperlipidaemia, Renal disease

METHODOLOGY

Each patient will be assessed by detailed history and clinical examination of both the eyes will be done by various methods as follows-

Setting- Ophthalmology Out Patient Department.

1) Visual acuity by Snellens chart for distant vision. (converted to logMAR)
2) Near vision.
3) Slit lamp bio microscopy.
4) Fundus examination by + 90D lens assisted slit lamp bio microscopy and indirect ophthalmoscopy.
5) Macular thickness using OCT
6) HbA1c levels
7) Random blood sugar level

The findings will be documented and patients found to have Diabetic macular oedema are identified.

Further they will be segregated and classified according to the severity of glycosylated hemoglobin levels.

Group 1 included HbA1c levels $\leq$7%

Group 2 included HbA1c levels between 7% and 8%

Group 3 included HbA1c levels $\geq$ 8%

The study subjects will be evaluated by OCT & the following parameters will be measured.

Central subfield macular thickness (mean 188.80 $\pm$27.64 µm)

Total macular volume (6.79 $\pm$ 0.392)

Central subfield macular thickness is the mean of retinal thickness values within central 1 mm diameter zone of foveola from six different radial scans.

Total macular volume is the volume in cubic millimeters of central 6 mm macula in retinal map analysis.[2]

The standard conventional OCT classification system requires understanding and assessment by a Vitreo-retina consultant. This simple thickness based grading system can be a useful tool for basic screening. Further evaluation by Vitreo-retina consultant can be planned for definite treatment.

SAMPLE SIZE ESTIMATION

Sample size variants estimate (27.64 µm) for central subfield macular thickness as reported in the study by Acta Ophthalmol. 2010: 88: 753–758, considering an absolute precision of 6µm around the mean.

Sample size (n)= $\frac{Z^2_{1-\alpha/2}\,\sigma^2}{d^2}$

Where,

σ: Standard Deviation

d: Precision

α/2 : desired confidence level

STATISTICAL METHODS USED FOR STUDY

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square was the test of significance. Continuous data was represented as mean and standard deviation. Paired t test was the test of significance to identify the mean difference between paired data. P value <0.05 was considered as statistically significant.

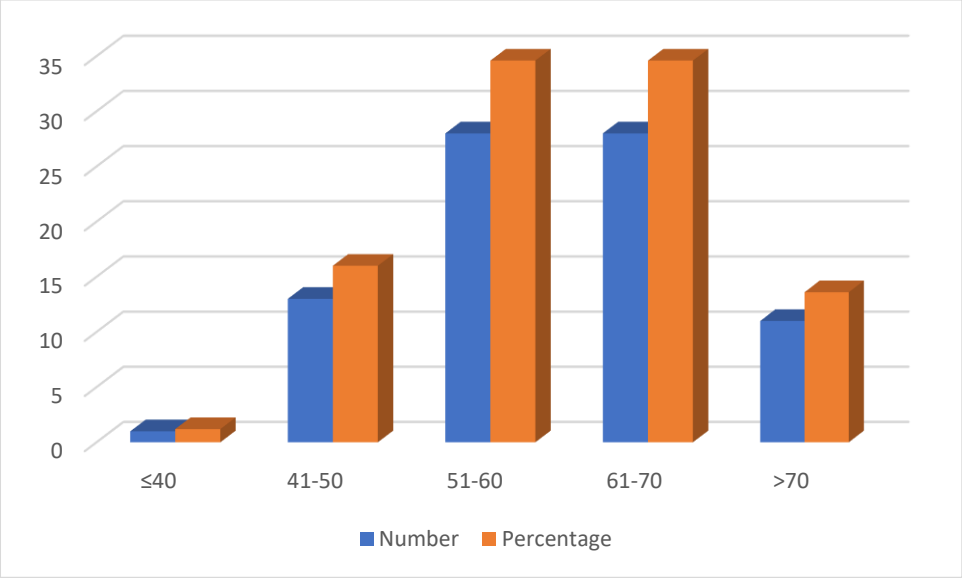
RESULTS

The present study was conducted for assessing the relationship between HbA1c levels and macular thickness in type 2 diabetic patients.

Table 1: Age-wise distribution of patients

Age group (years)	Number	Percentage
≤40	01	1.2
41-50	13	16.0
51-60	28	34.6
61-70	28	34.6
>70	11	13.6
Total	81	100.0
Mean ± SD	59.36 ± 8.98	
Range	40-81 years	

Graph 1: Age-wise distribution of patients

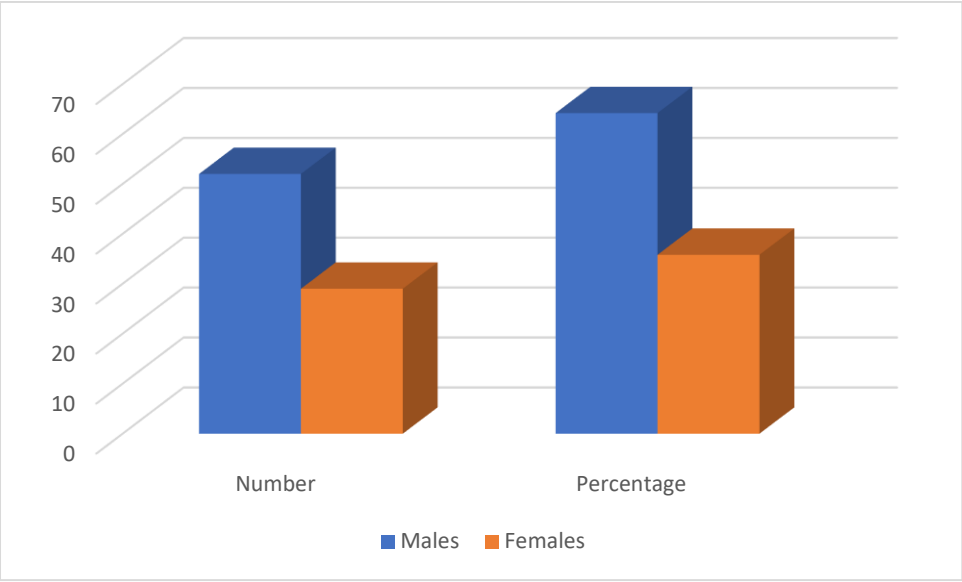


34.6 percent of the patients each belonged to the age group of 51 to 60 years and 61 to 70 years respectively, followed by 16 percent in the age group of 41 to 50 years. Mean age of the patients was 59.36 years.

Table 2: Gender-wise distribution of patients

Gender	Number	Percentage
Males	52	64.2
Females	29	35.8
Total	81	100.0

Graph 2: Gender-wise distribution of patients

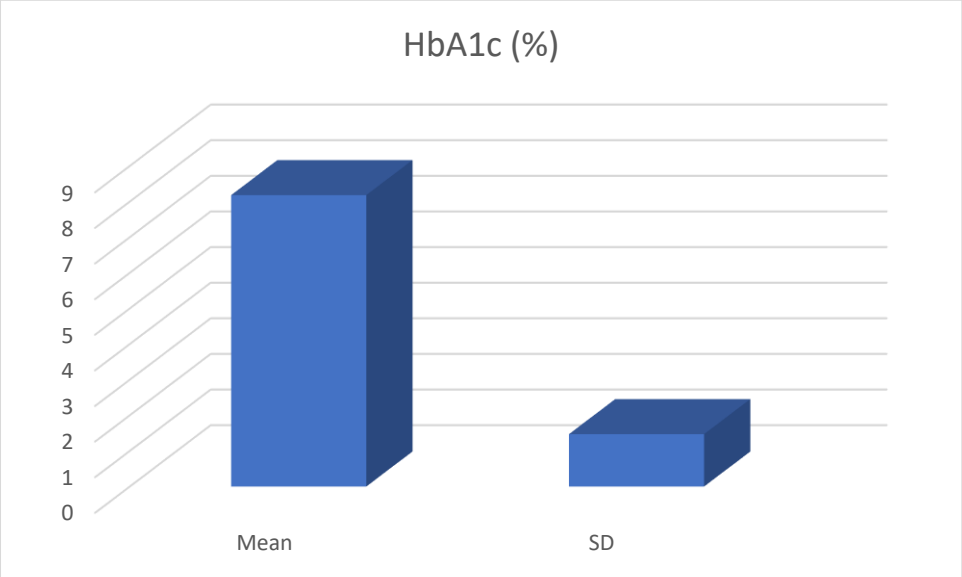


Out of 81 patients which were included in the study, 52 were males accounting for 64.2 percent of the patients, while the remaining 35.8 percent were females.

Table 3: Glycaemic profile

Glycaemic profile	Mean	SD	Range
HbA1c (%)	8.18	1.47	5.5-12.1

Graph 3: Glycaemic profile

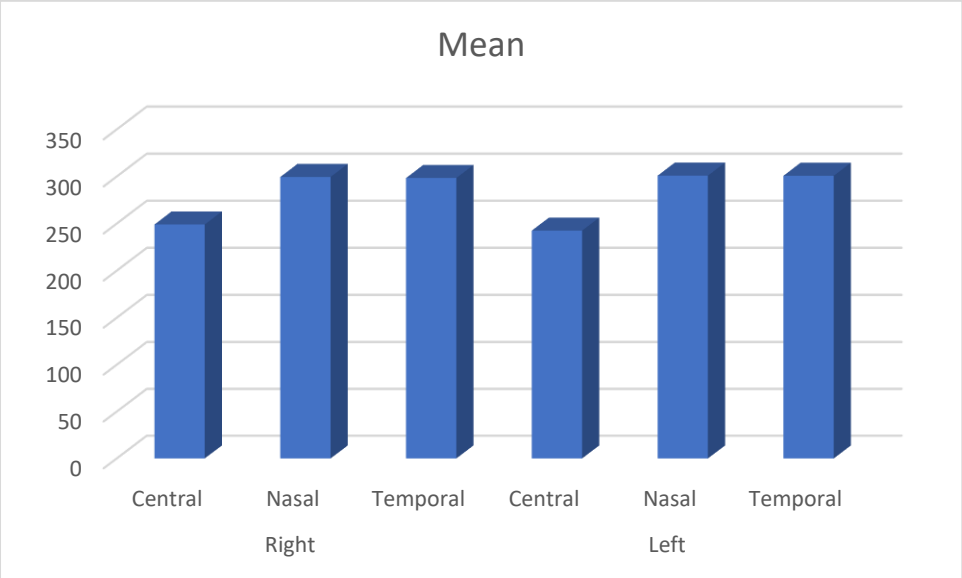


HbA1c values were in the range of 5.5-12.1 %. Mean HbA1c levels were found to be 8.18% with SD of 1.47

Table 4: Subfield thickness (µm)

Subfield thickness		**Mean**	**SD**	**Range**
Right	Central	249.05	49.09	157-357
	Nasal	299.49	53.29	196-456
	Temporal	298.42	46.55	180-416
Left	Central	242.54	64.21	99-425
	Nasal	300.88	64.81	141-594
	Temporal	300.76	52.09	138-399

Graph 4: Subfield thickness (µm)



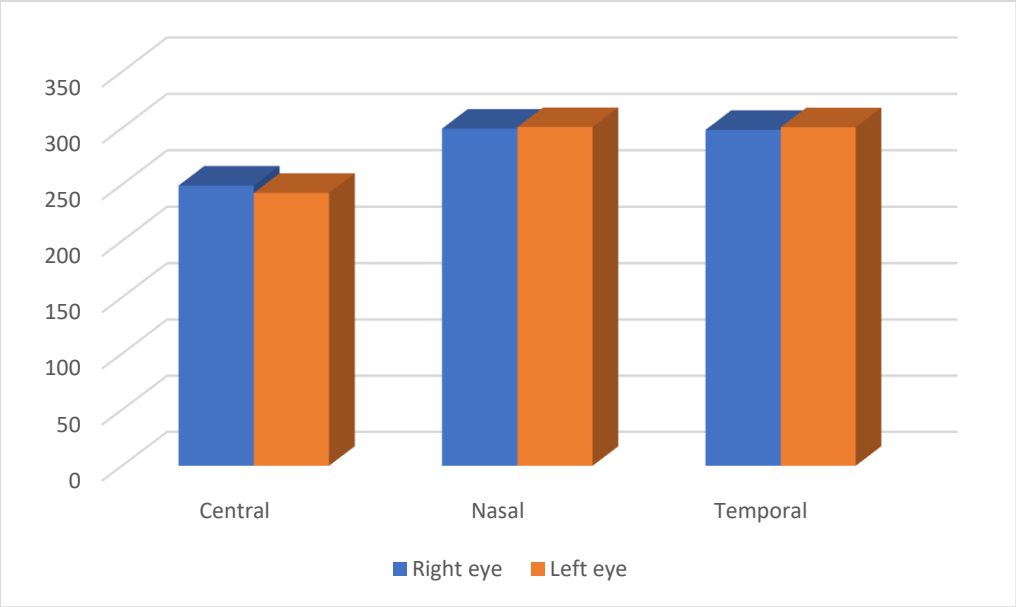
While analysing right eyes, mean subfield thickness at central, nasal and temporal region were found to be 249.05 µm, 299.49 µm and 298.42 µm respectively. While analysing left eyes, mean subfield thickness at central, nasal and temporal region were found to be 424.54 µm, 300.88 µm and 300.76 µm respectively.

Table 5: Comparison of subfield thickness between the right and left eye (µm) (Paired t test)

Subfield thickness	Right eye	Left eye	P value
Central	249.05±49.09	242.54±64.21	0.317
Nasal	299.49±53.29	300.88±64.81	0.820
Temporal	298.42±46.55	300.76±52.09	0.609

On comparing central, nasal and temporal subfield thickness between right eye and left eye, statistically insignificant results were obtained.

Graph 5: Comparison of subfield thickness between the right and left eye (µm) (Paired t test)



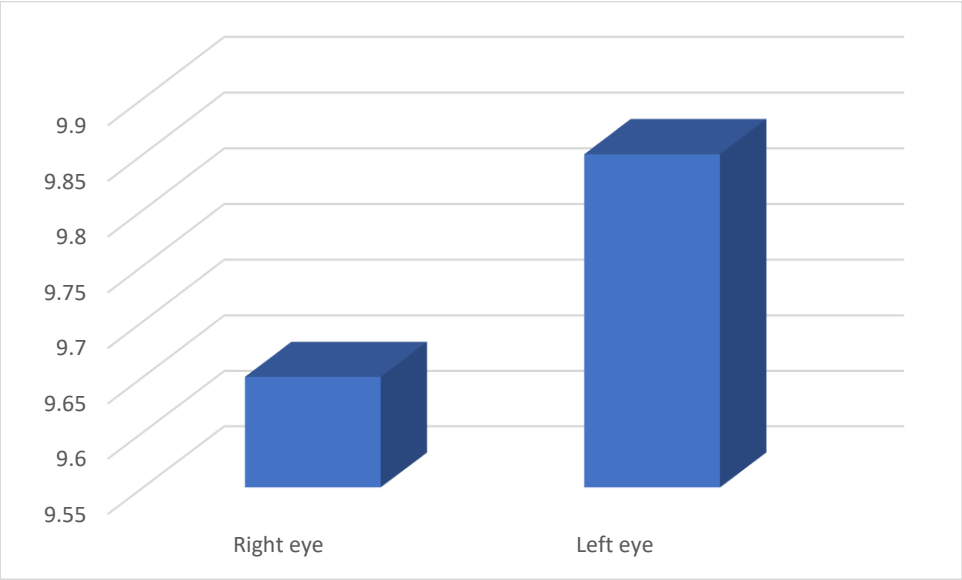
While comparing the subfield thickness in between right eye and left eye, non-significant results were obtained.

Table 6: Comparison of total macular volume between the right and left eye (µm) (Paired t test)

Variable	Mean	SD	Range	P value
Right eye	9.65	1.55	7.1-14.1	0.130
Left eye	9.85	1.62	6.9-15.3	

Mean macular volume among the left and right eye were found to be 9.65µm and 9.85µm respectively with SD of 1.55 and 1.62 respectively. On comparing statistically, the results were found to be statistically insignificant.

Graph 6: Comparison of total macular volume between the right and left eye (µm)



Mean macular volume among the left and right eye were found to be 9.65µm and 9.85µm respectively. On comparing statistically, the results were found to be statistically insignificant.

Table 7: Correlation between subfield thickness and HbA1C (Pearson Correlation)

Subfield thickness	**HbA1c**	**Correlation coefficient**	**P value**
Right eye	Central	0.635	0.001*
	Nasal	0.567	0.001*
	Temporal	0.428	0.001*
Left eye	Central	0.309	0.005*
	Nasal	0.472	0.001*
	Temporal	0.538	0.001*

*Statistically significant ($p<0.05$)

When HbA1c values were correlated with central, nasal and temporal subfield thickness among both left and right eyes, statistically significant results were obtained in both eyes with p value of 0.001 in all the groups except with left central subfield thickness where it was 0.005.

Table 8: Correlation between total macular volume and HbA1c (Pearson Correlation)

Total macular volume vs HbA1c	**Correlation coefficient**	**P value**
Right eye	0.463	0.001*
Left eye	0.462	0.001*

* Statistically significant ($p<0.05$)

Significant positive correlation was observed between total macular volume and HbA1c among both left and right eyes with p value of 0.001

Table 9: Correlation between age and HbA1c (Pearson Correlation)

Variable	**Correlation coefficient**	**P value**
Age vs HbA1c	0.291	0.008*

* Statistically significant ($p<0.05$)

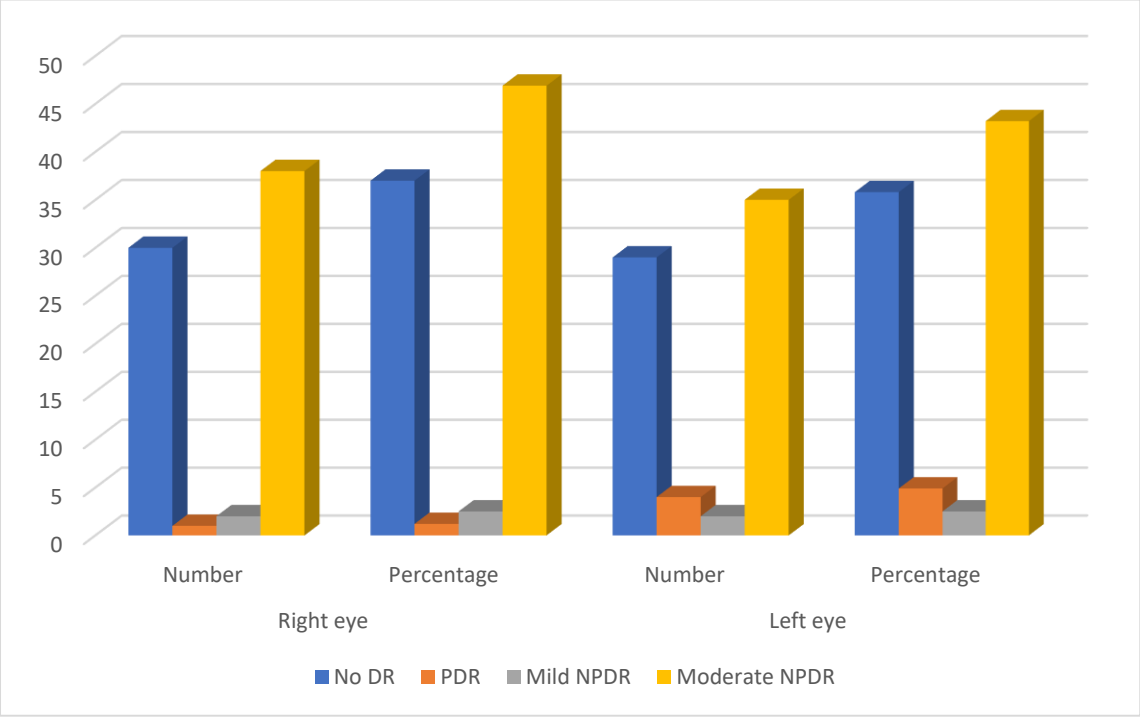
Significant positive correlation was observed between age and HbA1c.

Table 10: Grade of retinopathy changes in the right eye and left eye (Fisher Exact test)

Grade	Right eye		Left eye		P value
	Number	Percentage	Number	Percentage	
No DR	30	37	29	35.8	0.736
PDR	1	1.2	4	4.9	
Mild NPDR	2	2.5	2	2.5	
Moderate NPDR	38	46.9	35	43.2	
Severe NPDR	10	12.3	11	13.6	
Total	81	100	81	100	

Out of 81 patients included in the study, 38 patients had moderate NPDR changes in the right eye and 10 patients had severe NPDR changes while 30 patients showed no signs of retinopathy in the right eye. In left eye, 35 patients showed moderate NPDR changes, 11 showed severe NPDR changes, while 29 patients showed no signs of retinopathy.

Graph 7: Grade of retinopathy changes in the right eye and left eye (Fisher Exact test)



This is the graphical representation of the above table. No significant association was observed between the eye and grade of retinopathy

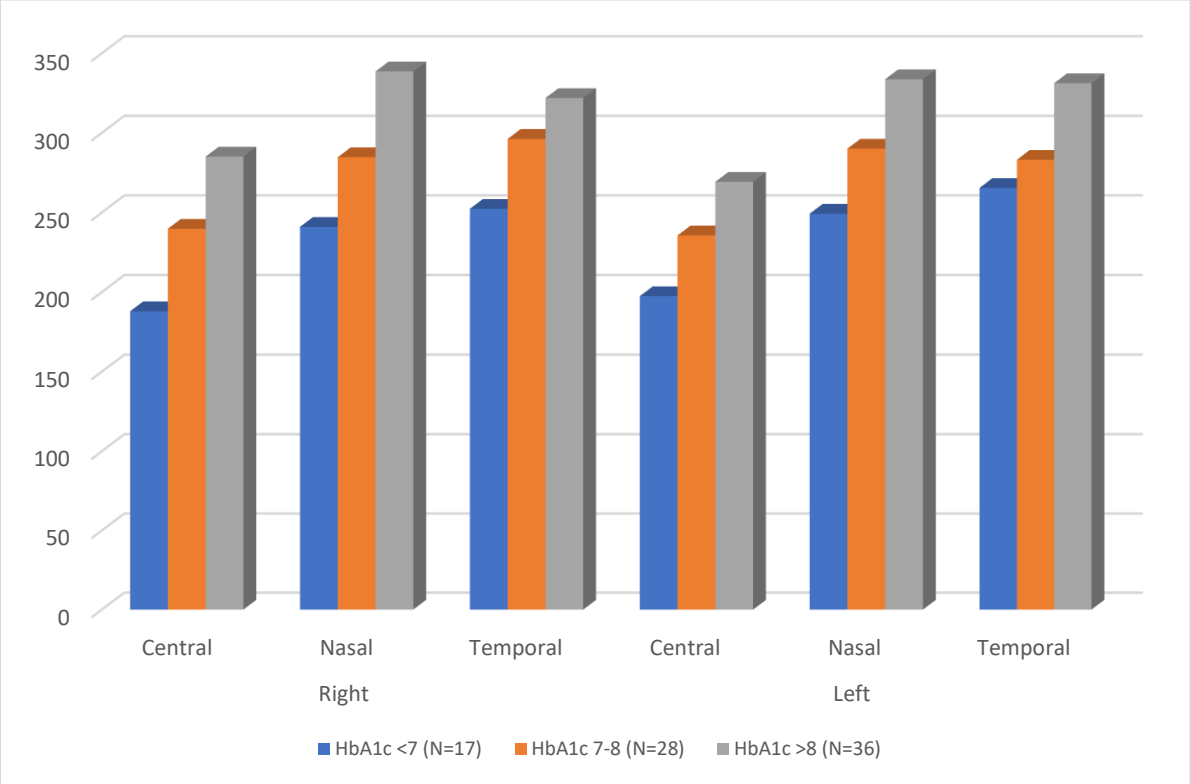
Table 11: Comparison of subfield thickness based on HbA1c (Analysis of Variance)

Subfield thickness		HbA1c			P value
		<7 (N=17)	**7-8 (N=28)**	**>8 (N=36)**	
Right	Central	187.94±33.16	239.78±30.93	285.11±32.38	0.001*
	Nasal	240.94±37.05	284.75±28.89	338.61±42.50	0.001*
	Temporal	252.29±29.57	296.25±31.34	321.88±46.82	0.001*
Left	Central	197.41±21.95	235.61±35.70	269.25±80.36	0.001*
	Nasal	249.23±23.61	290.11±30.07	333.67±78.44	0.001*
	Temporal	265.41±38.50	283.07±30.28	331.22±54.83	0.001*

*Statistically significant ($p<0.05$)

17 patients in our study had HbA1c value level below 7 while 28 and 36 patients had HbA1c levels between 7 to 8 and more than 8 respectively. When we compared central, nasal and temporal subfield thickness with HbA1c in these 3 groups, statistically significant results were obtained with p value of 0.001 in both eyes. Maximum thickness was seen temporally in both eyes, mean thickness being 321.88 μm and 331.22 μm in right and left eye respectively.

Graph 8: Comparison of subfield thickness based on HbA1c (Analysis of Variance)



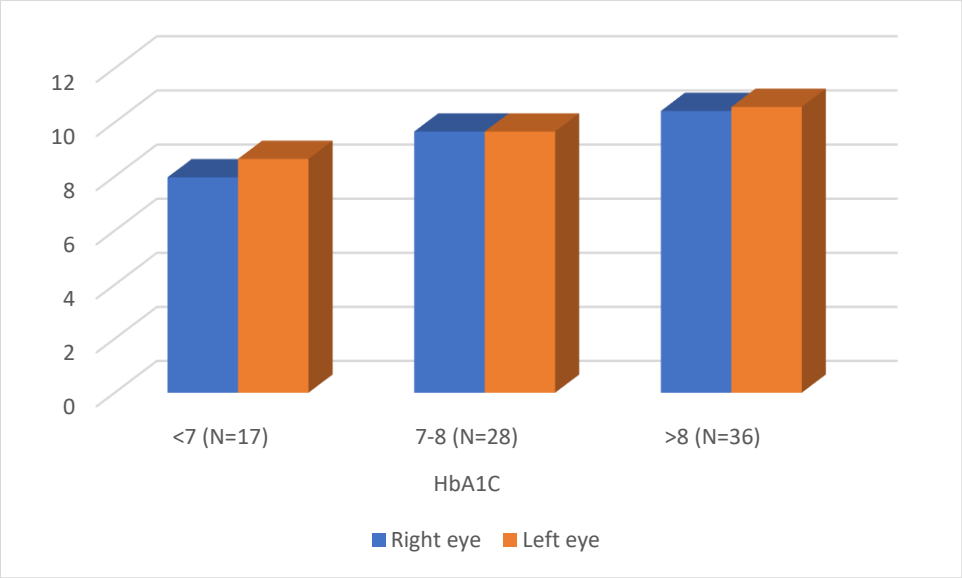
Subfield thickness (Central, nasal and temporal region) was significantly higher among patients with HbA1c value of more than 8 in comparison to patients with HbA1c value of less than 8; among both the left eyes and right eyes.

Table 12: Comparison of total macular volume based on HbA1c (Analysis of Variance)

Eye	HbA1C			P value
	<7 (N=17)	**7-8 (N=28)**	**>8 (N=36)**	
Right eye	7.97±1.11	9.66±0.84	10.42±1.54	0.001*
Left eye	8.65±1.21	9.66±1.02	10.57±1.81	0.001*

Total macular volume was significantly higher among patients with HbA1c value of more than 8 in comparison to patients with HbA1c value of less than 8; among both the left eyes and right eyes with p value of 0.001 in both eyes. It was lowest in patients with HbA1c values lower than 7.

Graph 9: Comparison of total macular volume based on HbA1c (Analysis of Variance)



Total macular volume was significantly higher among patients with HbA1c value of more than 8 in comparison to patients with HbA1c value of less than 8; among both the left eyes and right eyes with p value of 0.001 in both eyes.

Table 13: Correlation between age and subfield thickness (Pearson Correlation)

Age		Correlation coefficient	P value
	Central	0.286	0.010*
	Nasal	0.216	0.053
	Temporal	0.096	0.392
Left	Central	0.102	0.366
	Nasal	0.087	0.442
	Temporal	0.091	0.419

* Statistically significant ($p<0.05$)

Significant positive correlation was observed between right central subfield thickness only and age.

Table 14: Correlation between age and total macular volume (Pearson Correlation)

Age	Correlation coefficient	P value
Right eye	0.166	0.138
Left eye	0.145	0.198

Non-significant results were obtained while correlating age and total macular volume.

Table 15: Right and left eye subfield thickness based on retinopathy changes

Variable		Retinopathy changes (Mean ± SD)				
		No DR	**Mild NPDR**	**Moderate NPDR**	**Severe NPDR**	**PDR**
Right eye	Central	213.06±36.62	194.50±38.89	265.82±37.58	306.10±36.19	230.0
	Nasal	264.06±40.32	235.50±44.54	312.32±43.25	364.10±36.05	357
	Temporal	270.36±30.19	256.50±43.13	308.63±45.86	350.30±31.45	317
Left eye	Central	216.62±40.52	206.50±24.74	233.28±61.35	296.82±42.51	380.25±35.54
	Nasal	265.93±42.00	268.0±35.35	301.71±39.72	324.54±17.60	498.50±97.63
	Temporal	271.55±45.12	252.0±28.28	308.17±49.48	338.0±30.29	369.75±19.70

Graph 10: Right and left eye subfield thickness based on retinopathy changes

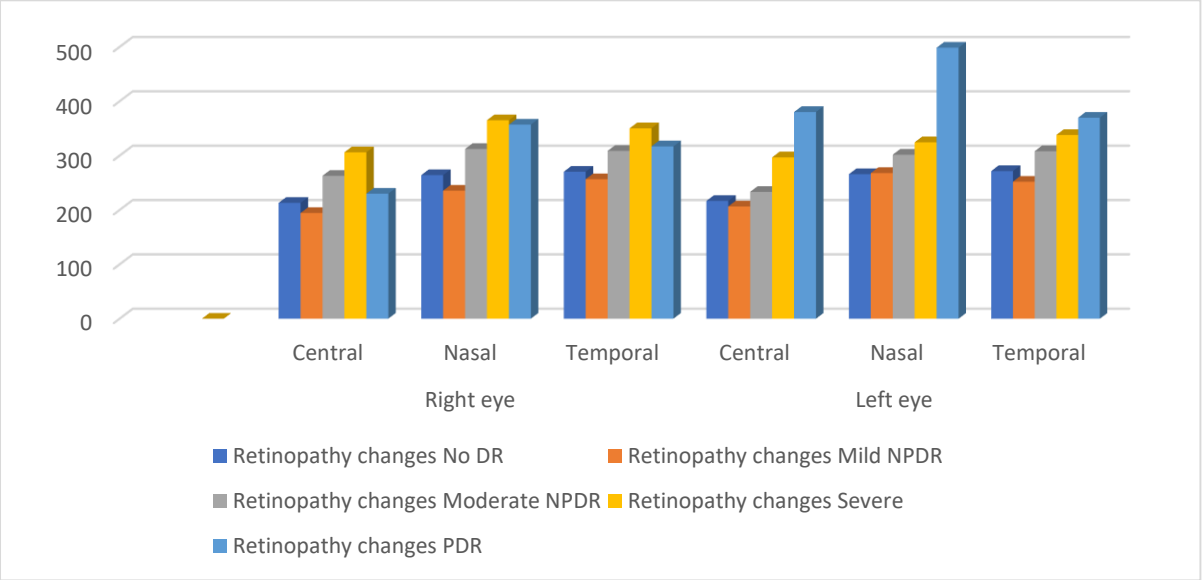


Table 16: Right and left eye total macular volume based on retinopathy changes

	Retinopathy changes (Mean±SD)				
	No DR	**Mild NPDR**	**Moderate NPDR**	**Severe NPDR**	**PDR**
Right eye	8.69±1.21	8.50±1.97	9.89±1.24	11.65±1.36	10.80
Left eye	9.03±1.43	8.50±1.69	9.88±0.99	10.70±1.23	14.0±0.88

Patients with PDR and severe NPDR showed higher levels of total macular volume in both eyes.

Graph 11: Right and left eye total macular volume based on retinopathy changes

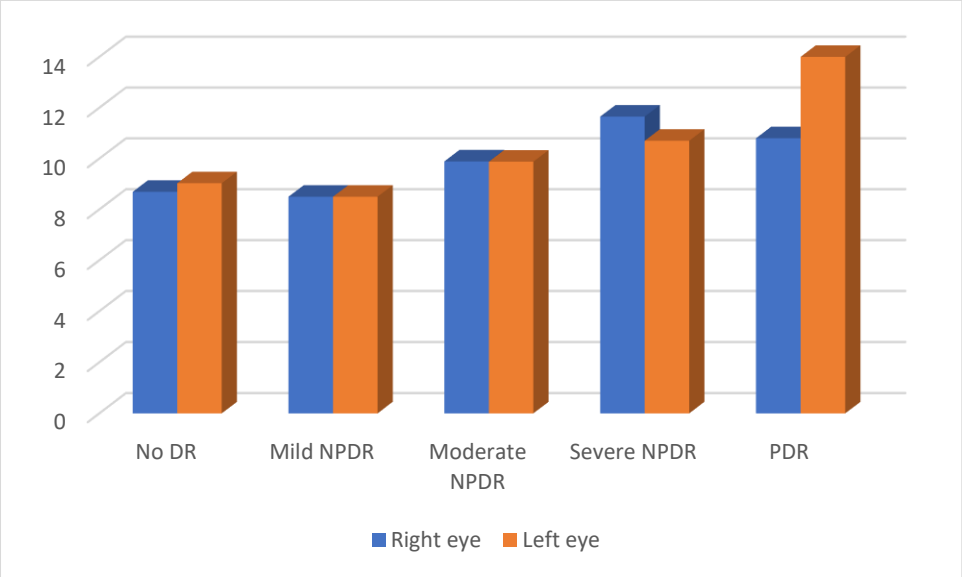


Table 17: Correlation between duration of diabetes and macular thickness (Pearson Correlation)

Age		Correlation coefficient	P value
Right	Central	0.223	0.046*
	Nasal	0.153	0.173
	Temporal	-0.003	0.976
Left	Central	0.066	0.561
	Nasal	0.040	0.725
	Temporal	-0.002	0.989

* Statistically significant ($p<0.05$)

Significant positive correlation was observed between duration of diabetes and right central macular thickness. A negative correlation is observed for right and left temporal macular thickness and duration of diabetes

Table 18: Correlation between duration of diabetes and HbA1c (Pearson Correlation)

Variable	Correlation coefficient	P value
Duration vs HbA1c	0.246	0.027

* Statistically significant ($p<0.05$)

Significant positive correlation was observed between duration of diabetes and HbA1c

DISCUSSION

DISCUSSION

Metabolic imbalance is a clinical feature of diabetes. There are an approximated three hundred and sixty-six million diabetics by 2030, up from one hundred and seventy one million in 2000. Diabetes affects individuals all over the globe. The most common source of visual impairment in working professionals is DR (diabetic retinopathy), that affects ⅓rd of diabetics in certain way. To enable prompt surveillance as well as recommendation, it is crucial to identify the earliest symptoms of diabetic retinopathy.[22- 24]

Initial stages of diabetic retinopathy do not exhibit any clinical characteristics. Slit-lamp biomicroscopy as well as stereo fundus photography, two common techniques for assessing this condition, are comparatively insensitive to minute pathologic alterations in the retina. Extremely sensitive fluorescein angiography is also invasive, therefore, not recommended for frequent testing.[22- 24]

As per the pathophysiology of DM in people, it is divided into insulin-dependent diabetes mellitus as well as noninsulin-dependent diabetes mellitus. The retinal width as well as structure among type 1 as well as type 2 diabetes mellitus failed to show a numerically noteworthy variation after adjusting for age, gender, period of diabetes as well as HbA1c concentrations, even though the pathomechanism as well as prevalence communities of the 2 forms are completely distinct. In usually, type 1 diabetes seems to have a protracted course,

but type 2 diabetes is a little older. As a result, such variables' potentially confusing effects may be used to measure retinal width.[22- 24]

The measurement of retinal width is nowadays routinely carried out using OCT (optical coherence tomography). There exist very few general community research papers on the patterns as well as relationships of OCT-measured retinal width, especially in white ethnicities, in regardless of extensive clinical use. Additionally, there are not many publications on normative OCT assessments in significant patient populations, including diabetics. To contrast, identify, as well as describe pathogenic alterations, normative data from general populations seem to be necessary. Since there will be around four hundred million people having diabetes globally by 2030, it is crucial to define normative values for them .[22- 24]

Hence; this research wascarried out for assessing the relationship among HbA1c concentrations as well as macular thickness in subjects having T2DM.

AGE

34.6 % of subjects each had their ages ranging from 51 - 60 years as well as 61 - 70 years accordingly. Our outcomes agreed with those attained by earlier researchers who have made comparable discoveries. In research carried out by **Jiang J et al**, mean age of patients was 64.4 years.[66]**Demir et al**, in another study, reported average age of subjects to be 55.06 years.[48] Mean age of the participants in another research conducted by **Chou TH et al** was 62.8 years.[44]

GENDER

64.2 percent of the patients comprised of men whereas the rest were women. Our outcomes were in agreement with those attained by earlier researchers who have made comparable discoveries. In research carried out by **Chou TH et al**, 64.7% of subjects were males.[44]Another research carried out by **Teberik et al** showed that 54.55 percent of the patients were males.[67]

GLYCAEMIC PROFILE

Mean HbA1c levels were found to be 8.18%. Mean HbA1c levels in a research carried out by **Jiang J et al** among those having diabetic retinopathy was 9.3 percent.[66]**Demir et al**, in a different research reported mean HbA1c concentrations to be 8.92%.[48] In a research carried out by **Kocak Altintas AG et al**, the mean HbA1c value seemed to be 8.67%.[68]

SUBFIELD THICKNESS (MM)

While analysing right eyes, mean subfield at central, nasal and temporal region were found to be 249.05 μm, 299.49 μm and 298.42 μm respectively. While analysing left eyes, mean subfield at central, nasal and temporal region were found to be 424.54 μm, 300.88 μm and 300.76 μm accordingly. In a research carried out by **Jiang J et al**, while analysing right eyes, mean subfield at central, nasal and temporal region were found to be 258.4 μm, 334.3 μm and 319.9 μm respectively. While analysing left eyes, mean subfield at central, nasal and temporal region were found to be 258.4 μm, 307.4 μm and 276.4 μmcorrespondingly.[66- 68]

RIGHT AND LEFT EYE (MM)

While comparing the subfield thickness in between right eye and left eye, non-significant results were obtained. Mean macular volume among the left and right eye were discovered to be 9.65 **micrometre** and 9.85 **micrometre** accordingly. On comparing statistically, the results were found to be numerically noteworthy.

ASSOCIATION AMONG SUBFIELD WIDTH AS WELL AS HBA1C

Significant positive association was observed among central subfield width (Central, Nasal, Temporal) as well as HbA1c among both left and right eyes. Alterations in retinal widthas a consequence ofDM are not completely understood. Earlier investigations have discovered reduced retinal width in DMhaving little or no diabetic retinopathy in contrast to retinal width in nondiabetic people. (**Chen Y et al**). Comparatively, other studies have noted a propensity towards greater retinal widths in those having developed retinopathy (**Park HY et al, Pires I et al**).[69- 70]

ASSOCIATION AMONG TOTAL MACULAR VOLUME AS WELL AS HBA1C

Significant positive association was observed among total macular volume and HbA1c among both left and right eyes. Our outcomes were in agreement with those of **Demir and his co-workers** who also reported significantly positive association among total macular volume as well as HbA1c.[48]

A variation in OCT measures more than ten percent of the reference width is expected to indicate a significant alteration in macular width, according to research by **Browning et al**. as

well as **Hee et al**. A criterion which may be applied to track long-term diabetes is glycosylated hemoglobin. [72], [73] Elevated baseline HbA1c as well as a significant drop in HbA1c, according to **Moon et al**., constituted risk variables for the development of macular thinning. [47] **Yeung et al**. demonstrated a favorable correlation between HbA1c concentration as well as macular width in subjects having type 1 as well as type 2 diabetes for at least ten years lacking diabetic macular edema.[45]

Chou et al. demonstrated that among diabetic individuals having diabetic retinopathy, a HbA1c value of eight percent or higher was linked to an increment in retinal width. [44] According to **Yeung et al., Chou et al., as well as Rosenstock et al**., strict diabetes management might help to minimize macular malfunction as well as slow the development of initial diabetic retinopathy. Careful monitoring of plasma sugar levels in people with type 1 as well as type 2 diabetes may slow the growth as well as onset of diabetic retinopathy. [44] [45] [74]

COMPARISON OF SUBFIELD THICKNESS BASED ON HBA1C

Subfield thickness (Central, nasal and temporal region) was significantly higher among subjects having HbA1c value of over 8 in comparison to patients having HbA1c value of below 8; among both the left as well as right eyes. In a research carried out by **Jiang J et al**, following adjustment for age as well as gender, the Pearson correlation analysis discovered that just the temporal perifoveal width possessed a negative association with HbA1c content, hence demonstrating that an elevated HbA1c content lead to reduced retinal width.[66]

The pathophysiological mechanisms behind diabetic retinopathy are intricate as well as multifaceted. When anatomical as well as functional anomalies of retina are absent in the

initial phases of diabetic retinopathy, vascular malfunction might still arise. Because of its higher cone density, the fovea seems to have a higher metabolic need. (Jiang J et al).[66]

As stated by **Yau et al**, advancement of severity of DR is predicted by HbA1c status.[75]Inverse correlation of Retinal thickness with glycaemic profile (as assessed by glycated haemoglobin) is also established (**Asefzadeh B et al**).[76] A research conducted by **Brynskov T et al** demonstrated that a decline in glycaemic profile is accompanied by thickening of inner retinal layers in the parafovea after bariatric surgery.[77] In the current research also, an inverse association of retinal thickness with glycaemic profile was observed.

COMPARISON OF TOTAL MACULAR VOLUME BASED ON HBA1C

Total macular volume was significantly higher among subjects having HbA1c value of over 8 in comparison to subjects having HbA1c value under 8; among both the left eyes and right eyes.

In contrast to the control group, **Bhavsar** as well as **Subramaniam** discovered that a considerable proportion of subjects having subclinical macular oedema eventually advance to clinically noteworthy macular oedema, having the chances of progression increasing by fifteen percent for every ten micrometre rise in central subfield macular width. It might be crucial to supervise these diabetes patients more carefully in order to identify macular oedema which could damage their vision earlier.[78]

ASSOCIATE AMONG PERIOD OF DIABETES AS WELL AS MACULAR WIDTH

A considerable positive association was noted among the period of diabetes as well as right central macular thickness. A negative correlation is observed for right and left temporal macular width as well astime period of DM.

CORRELATION BETWEEN DURATION OF DIABETES AND HBA1C

The time span of diabetes as well as HbA1c showed a strong positive association. Initial-stage DM patients reduced retinal widths were a reflection of neurodegenerative alterations in their retinas, including glial cell absence or degradation. In individuals having peripheral neuropathy, **Srinivasan et al**. have noted reduced widths in parafovea as well as perifovea. Neurodegeneration might have accelerated vascular permeability on the advancement of the condition, that could have resulted in increased width of retinal layers.[79]

In comparison to patients who didn't have diabetic retinopathy as well as non-diabetics, **Sng CCA et al**. found that diabetics having moderate or extreme retinopathy exhibited greater fovea as well as temporal outer macular width. This could be described by a change in the BRB (blood retinal barrier) in mild to moderate diabetic retinopathy, that might allow for an elevation of the vascular permeability of macular as well as perifoveal capillaries. Interstitial oedema related to perifoveal capillary loss, that has been observed to emerge in the progression of retinopathy, is yet another potential reason for increasing foveal width in those having moderate or extreme retinopathy. [8082]

In regions showing macular oedema, the blood circulation was revealed to be relatively low by **Hudson et al**. This decrease was more noticeable in temporal rather than nasal macula,

that is constant with our observation that subjects having moderate to extreme retinopathy had thicker temporal outer maculae. Despite the lack of oedema, such vascular alterations might be linked to the degree of diabetic retinopathy. It will take more research to confirm such theories. OCT can identify macular thickness faster than clinical assessment, according to a meta-analysis examining the diagnostic efficacy of OCT for identifying macular oedema in persons having DR, however most of these instances did not advance to clinically apparent oedema as well as required photocoagulation. [83] [84]

Unsal et al. additionally discovered a connection between the average HbA1c concentrations, that stood over eight percent in the NPDR cohort, over nine percent in the eyes having PDR, & nine percent in the DME cohort, as well as the diabetic retinopathy phase, macular inclusion along with blood sugar concentrations. The HbA1c score was determined to be beyond the typical upper limits by **Sasaki et al.** after evaluating seventy-four patients having no diabetic retinopathy as well as seven subjects with relatively minor retinopathy. HbA1c levels were greater in eyes having DME as compared to eyes lacking DME,according to **Cetin et al**. In the research by **Jew et al**., multivariate assessment revealed that HbA1c concentrations were among the primary risk factors for acquiring CSME. [67] [85] [88]

Seven hundred and forty-eight diabetic individuals volunteered in **Su et al's** study of the relationship among diabetes & hyperglycemia as well as CCT in three thousand two hundred and thirty nine eyes, and the results revealed a CCT that was six and a half micrometers wider than that of the non-diabetic participants in the reference cohort. After analyzing the CCT among diabetic subjects having normal fundus as well as DR background, Lee et al. discovered that CCT seemed to be greater in those having diabetes compared to the reference population. According to **Inoue et al. & Choo et al**., CCT results for the diabetic population did not demonstrate any appreciable variation from reference cohort. The research by

Ozdamar et al. revealed that the CCT readings in the diabetes category were substantially greater than those in the control group. HbA1c as well as CCT do not correlate, according to the same research.

Whilst HbA1c is indeed a measure of long-term treatment of diabetes mellitus, we believe that elevated blood sugar concentrations are more likely to cause corneal thickness throughout a diabetic subject's lifetime. [89] [93]

CONCLUSION

CONCLUSION

- Our observations provide cross-sectional data that might to be of utmost utility for assessing and evaluating macular thickness among diabetic subjects.

- Current results demonstrate that CMT is significantly elevated among DR subjects with moderate to severe levels of severity even in the absence of DME.

- Further researches by employing spectral-domain OCT should be conducted for better exploration of the observations of the present study.Higher and advanced retinal segmentation techniquescould be employed for assessing whether specific retinal layers are preferentially affected by DM.

SUMMARY

SUMMARY

Complications of Diabetes mellitus (DM) often are the result of long-term exposure to high blood glucose levels brought on by abnormalities in insulin metabolism and biological macromolecules. Diabetes can cause macular edema in a variety of ways. With the help of optical coherence tomography (OCT), assessment of macula's structures can be carried out more thoroughly.

Hence; 81 patients with Type 2 Diabetic mellitus visiting the outpatient department of Ophthalmology at R.L.J Hospital and Research Centre, attached to Sri Devaraj Urs Medical College between January 2021 and September 2022, after obtaining the approval from Institutional Ethics Committee were enrolled with the aim of assessing the relationship between glycosylated hemoglobin levels and macular thickness on optical coherence tomography in type 2 diabetic patients.

Mean age of the patients was 59.36 years with majority proportion of patients being male population. No significant results were obtained while comparing the subfield thickness in between right eye and left eye, non-significant results were obtained.

Mean macular volume among the left and right eye were found to be 9.65 μm and 9.85 μm respectively; which on comparing statistically were found to be significant. Also; we observed significant high positive correlation between central subfield thickness (Central, Nasal, Temporal) and HbA1c among both left and right eyes and also between total macular volume and HbA1c among both left and right eyes.

However; we did not observe any significant association between the eye and grade of retinopathy. Subfield thickness (Central, nasal and temporal region) was significantly higher among patients with HbA1c value of more than 8 in comparison to patients with HbA1c value of less than 8; among both the left eyes and right eyes.

Total macular volume was significantly higher among patients with HbA1c value of more than 8 in comparison to patients with HbA1c value of less than 8; among both the left eyes and right eyes. Significant positive correlation was observed between right central subfield thickness only and age. Non-significant results were obtained while correlating age and total macular volume. Significant positive correlation was observed between duration of diabetes and right central macular thickness. A negative correlation is observed for right and left temporal macular thickness and duration of diabetes

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ANNEXURE-I

CASE PROFORMA

CASE PROFORMA	
Name:	Case No:
Age:	Date:
Sex:	OP No:
Occupation:	DOE:
Address:	

Chief complaints:

H/O presenting illness:

Past history:

DM / HTN / BA / Epilepsy

Family history:

Personal history:

Appetite – Sleep – Bowel –

Diet – Habits – Bladder –

GPE:

Pallor / Edema /Icterus / Cyanosis / Clubbing / Lymphadenopathy

Vital signs:

a. Pulse – c) RR –

b. BP – d) Temp –

Systemic examination:

a. CVS – c. RS –

b. PA – d. CNS –

OCULAR EXAMINATION		
TESTS	**RE**	**LE**
HEAD POSTURE OCULAR POSTURE FACIAL SYMMETRY		
EXTRAOCULAR MOVEMENTS Ductions Versions		
VISUAL ACUITY: Distant Near		
ANTERIOR SEGMENT		
FUNDUS Distant direct ophthalmoscopy Direct ophthalmoscopy Indirect ophthalmoscopy		
OCT 1. CSMT 2. TMV		
INVESTIGATIONS 1. HbA1c 2. RBS 3. FBS 4. PPBS		

ANNEXURE-II

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101

PATIENT INFORMATION SHEET

PATIENT INFORMATION SHEET

This information is to help you understand the purpose of the study "**RELATIONSHIP BETWEEN GLYCOSYLATED HEMOGLOBIN LEVELS AND MACULAR THICKNESS ON OPTICAL COHERENCE TOMOGRAPHY IN TYPE II DIABETIC PATIENTS**". You are invited to take part voluntarily in this research study, it is important that you read and understand the purpose, procedure, benefits and discomforts of the study.

Uncontrolled Type II diabetes mellitus causes thickening of the retina which causes gradual loss of vision. The purpose of this study is to find out the changes that might have occurred due to diabetes in the retina. Relation between HbA1c levels and macular thickness on Optical Coherence Tomography will be analysed.If you are willing to take part in this study, you need to give clinical information and following procedures will be carried out:

1. Visual acuity by Snellens chart for distant vision(converted to logMAR)
2. Near vision – jaeger chart.
3. Slit lamp biomicroscopy.
4. Fundus examination by 90D slit lamp biomicroscopy and indirect ophthalmoscopy, including optic disc evaluation.
5. Macular thickness on OCT
6. HbA1c levels
7. Random blood sugar levels.

You will not be charged for any of the tests. All the tests are routine tests and absolutely no risks are associated with various investigations.

If during the procedure, any unexpected event occurs like redness of eyes, itching, blurring, Doctor will take care of it.

If you participate in the study, the generated data might be helpful for further treatment protocol or to avoid complications. The collected data will be used for presentation in medical conferences and identity will not be revealed. Your medical information will be kept confidential by the study doctor and staff and will not be made publicly available. Your original records may be reviewed by your doctor or ethics review board.

You may refuse to take part in the study or you may stop your participation in the study at any time, without a penalty or loss of any benefits to which you were otherwise entitled before taking part in this study.

Extra monetary benefits or money will not be paid for taking part in the study.

For further information / clarification please contact

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SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.

ಶ್ರೀ ದೇವರಾಜ್ ಅರ್ಸ್ ಉನ್ನತ ಶಿಕ್ಷಣ ಮತ್ತು ಸಂಶೋಧನೆ ಅಕಾಡೆಮಿ, ತಮಕ,

ಕೋಲಾರ - 563101

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

1. "ಟೈಪ್ II ಡಯಾಬಿಟಿಕ್ ರೋಗಿಗಳಲ್ಲಿ ಆಪ್ಟಿಕಲ್ ಕೊಹೆರೆನ್ಸ್ ಟೊಮೊಗ್ರಫಿಯಲ್ಲಿ ಗ್ಲೈಕೋಸೈಲೇಟೆಡ್ ಹಿಮೋಗ್ಲೋಬಿನ್ ಮಟ್ಟಗಳು ಮತ್ತು ಮ್ಯಾಕ್ಯುಲರ್ ದಪ್ಪದ ನಡುವಿನ ಸಂಬಂಧ" ಅಧ್ಯಯನದ ಉದ್ದೇಶವನ್ನು ಅರ್ಥಮಾಡಿಕೊಳ್ಳಲು ಈ ಮಾಹಿತಿಯು ನಿಮಗೆ ಸಹಾಯ ಮಾಡುತ್ತದೆ. ಈ ಸಂಶೋಧನಾ ಅಧ್ಯಯನದಲ್ಲಿ ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಪಾಲ್ಗೊಳ್ಳಲು ನಿಮ್ಮನ್ನು ಆಹ್ವಾನಿಸಲಾಗಿದೆ, ಅಧ್ಯಯನದ ಉದ್ದೇಶ, ಕಾರ್ಯವಿಧಾನ, ಪ್ರಯೋಜನಗಳು ಮತ್ತು ಅನಾನುಕೂಲಗಳನ್ನು ನೀವು ಓದುವುದು ಮತ್ತು ಅರ್ಥಮಾಡಿಕೊಳ್ಳುವುದು ಮುಖ್ಯವಾಗಿದೆ.
2. ಅನಿಯಂತ್ರಿತ ಟೈಪ್ II ಡಯಾಬಿಟಿಸ್ ಮೆಲ್ಲಿಟಸ್ ರೆಟಿನಾದ ದಪ್ಪವಾಗಲು ಕಾರಣವಾಗುತ್ತದೆ, ಇದು ಕ್ರಮೇಣ ದೃಷ್ಟಿ ಕಳೆದುಕೊಳ್ಳುತ್ತದೆ. ರೆಟಿನಾದಲ್ಲಿ ಮಧುಮೇಹದಿಂದ ಉಂಟಾಗಬಹುದಾದ ಬದಲಾವಣೆಗಳನ್ನು ಕಂಡುಹಿಡಿಯುವುದು ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶವಾಗಿದೆ. ಆಪ್ಟಿಕಲ್ ಕೊಹೆರೆನ್ಸ್ ಟೊಮೊಗ್ರಫಿಯಲ್ಲಿ HbA1c ಮಟ್ಟಗಳು ಮತ್ತು ಮ್ಯಾಕ್ಯುಲರ್ ದಪ್ಪದ ನಡುವಿನ ಸಂಬಂಧವನ್ನು ವಿಶ್ಲೇಷಿಸಲಾಗುತ್ತದೆ. ನೀವು ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಸಿದ್ಧರಿದ್ದರೆ, ನೀವು ಕ್ಲಿನಿಕಲ್ ಮಾಹಿತಿಯನ್ನು ನೀಡಬೇಕಾಗುತ್ತದೆ ಮತ್ತು ಕೆಳಗಿನ ಕಾರ್ಯವಿಧಾನಗಳನ್ನು ಕೈಗೊಳ್ಳಲಾಗುತ್ತದೆ:
    1. ದೂರದ ದೃಷ್ಟಿಗಾಗಿ ಸ್ನೆಲೆನ್ಸ್ ಚಾರ್ಟ್‌ನಿಂದ ದೃಷ್ಟಿ ತೀಕ್ಷ್ಣತೆ (ಲಾಗ್‌ಮಾರ್‌ಗೆ ಪರಿವರ್ತಿಸಲಾಗಿದೆ)
    2. ಸಮೀಪ ದೃಷ್ಟಿ – ಜೇಗರ್ ಚಾರ್ಟ್.
    3. ಸ್ಲಿಟ್ ಲ್ಯಾಂಪ್ ಬಯೋಮೈಕ್ರೋಸ್ಕೋಪಿ.
    4. ಆಪ್ಟಿಕ್ ಡಿಸ್ಕ್ ಮೌಲ್ಯಮಾಪನ ಸೇರಿದಂತೆ 90D ಸ್ಲಿಟ್ ಲ್ಯಾಂಪ್ ಬಯೋಮೈಕ್ರೋಸ್ಕೋಪಿ ಮತ್ತು ಪರೋಕ್ಷ ನೇತ್ರದರ್ಶಕದಿಂದ ಫಂಡಸ್ ಪರೀಕ್ಷೆ.
    5. OCT ನಲ್ಲಿ ಮ್ಯಾಕ್ಯುಲರ್ ದಪ್ಪ
    6. HbA1c ಮಟ್ಟಗಳು
    7. ಯಾದೃಚ್ಛಿಕ ರಕ್ತದಲ್ಲಿನ ಸಕ್ಕರೆ ಮಟ್ಟಗಳು.

ಯಾವುದೇ ಪರೀಕ್ಷೆಗಳಿಗೆ ನಿಮಗೆ ಶುಲ್ಕ ವಿಧಿಸಲಾಗುವುದಿಲ್ಲ. ಎಲ್ಲಾ ಪರೀಕ್ಷೆಗಳು ವಾಡಿಕೆಯ ಪರೀಕ್ಷೆಗಳು ಮತ್ತು ಸಂಪೂರ್ಣವಾಗಿ ಯಾವುದೇ ಅಪಾಯಗಳು ವಿವಿಧ ತನಿಖೆಗಳೊಂದಿಗೆ ಸಂಬಂಧ ಹೊಂದಿಲ್ಲ.

ಕಾರ್ಯವಿಧಾನದ ಸಮಯದಲ್ಲಿ, ಕಣ್ಣುಗಳು ಕೆಂಪಾಗುವುದು, ತುರಿಕೆ, ಮಸುಕು ಮುಂತಾದ ಯಾವುದೇ ಅನಿರೀಕ್ಷಿತ ಘಟನೆ ಸಂಭವಿಸಿದಲ್ಲಿ, ವೈದ್ಯರು ಅದನ್ನು ನೋಡಿಕೊಳ್ಳುತ್ತಾರೆ.

ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಿದರೆ, ರಚಿತವಾದ ಡೇಟಾವು ಹೆಚ್ಚಿನ ಚಿಕಿತ್ಸಾ ಪ್ರೋಟೋಕಾಲ್‌ಗೆ ಅಥವಾ ತೊಡಕುಗಳನ್ನು ತಪ್ಪಿಸಲು ಸಹಾಯಕವಾಗಬಹುದು. ಸಂಗ್ರಹಿಸಿದ ಡೇಟಾವನ್ನು ವೈದ್ಯಕೀಯ ಸಮ್ಮೇಳನಗಳಲ್ಲಿ ಪ್ರಸ್ತುತಿಗಾಗಿ ಬಳಸಲಾಗುತ್ತದೆ ಮತ್ತು ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿಯನ್ನು ಅಧ್ಯಯನ ವೈದ್ಯರು ಮತ್ತು ಸಿಬ್ಬಂದಿ ಗೌಪ್ಯವಾಗಿಡುತ್ತಾರೆ ಮತ್ತು ಸಾರ್ವಜನಿಕವಾಗಿ ಲಭ್ಯವಾಗುವಂತೆ ಮಾಡಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಮೂಲ ದಾಖಲೆಗಳನ್ನು ನಿಮ್ಮ ವೈದ್ಯರು ಅಥವಾ ಎಥಿಕ್ಸ್ ರಿವ್ಯೂ ಬೋರ್ಡ್ ಪರಿಶೀಲಿಸಬಹುದು.

ನೀವು ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳಲು ನಿರಾಕರಿಸಬಹುದು ಅಥವಾ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವ ಮೊದಲು ನೀವು ಅರ್ಹರಾಗಿದ್ದ ಯಾವುದೇ ಪ್ರಯೋಜನಗಳ ದಂಡ ಅಥವಾ ನಷ್ಟವಿಲ್ಲದೆಯೇ ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವುದನ್ನು ನಿಲ್ಲಿಸಬಹುದು.

ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಿದ್ದಕ್ಕಾಗಿ ಹೆಚ್ಚುವರಿ ವಿತ್ತೀಯ ಪ್ರಯೋಜನಗಳು ಅಥವಾ ಹಣವನ್ನು ಪಾವತಿಸಲಾಗುವುದಿಲ್ಲ.

ಹೆಚ್ಚಿನ ಮಾಹಿತಿಗಾಗಿ / ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ದಯವಿಟ್ಟು ಸಂಪರ್ಕಿಸಿ

ಡಾ. ವೃಷಭ್ ಮಲಾನಿ (ಸಂಪರ್ಕ ಸಂಖ್ಯೆ: 8668415144, 9403396110)

ಜೂನಿಯರ್ ನಿವಾಸಿ

ನೇತ್ರಶಾಸ್ತ್ರ ವಿಭಾಗ,

ಶ್ರೀ ದೇವರಾಜ್ ಅರ್ಸ್ ಉನ್ನತ ಶಿಕ್ಷಣ ಮತ್ತು ಸಂಶೋಧನೆ ಅಕಾಡೆಮಿ,

ತಮಕ, ಕೋಲಾರ - 563101.

ANNEXURE-III

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR - 563101.

INFORMED CONSENT FORM

Case no:

IP no:

TITLE: RELATIONSHIP BETWEEN GLYCOSYLATED HEMOGLOBIN LEVELS AND MACULAR THICKNESS ON OPTICAL COHERENCE TOMOGRAPHY IN TYPE II DIABETIC PATIENTS

I, the undersigned, agree to participate in this study and authorize the collection and disclosure of personal information as outlined in this consent form. I was told in the language I understand.

I understand the purpose of this study, the risks and benefits of the technique and the confidential nature of the information that will be collected and disclosed during the study. The information collected will be used only for research.

I have had the opportunity to ask questions regarding the various aspects of this study and my questions have been answered to my satisfaction.

I understand that I remain free to withdraw the participation from this study at any time and this will not change the future care.

Participation in this study does not involve any extra cost to me.

Name	Signature	Date	Time
Patient:			
Witness:			
Primary Investigator/ Doctor:			

ಶ್ರೀ ದೇವರಾಜ್ ಅರ್ಸ್ ಉನ್ನತ ಶಿಕ್ಷಣ ಮತ್ತು ಸಂಶೋಧನೆ ಅಕಾಡೆಮಿ, ತಮಕ,

ಕೋಲಾರ - 563101

<u>ಮಾಹಿತಿ ನೀಡಿದ ಒಪ್ಪಿಗೆ ನಮೂನೆ</u>

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ನಾನು, ಕೆಳಗೆ ಸಹಿ ಮಾಡಿದ್ದೇನೆ, ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ಒಪ್ಪುತ್ತೇನೆ ಮತ್ತು ಈ ಸಮ್ಮತಿ ನಮೂನೆಯಲ್ಲಿ ವಿವರಿಸಿದಂತೆ ವೈಯಕ್ತಿಕ ಮಾಹಿತಿಯ ಸಂಗ್ರಹಣೆ ಮತ್ತು ಬಹಿರಂಗಪಡಿಸುವಿಕೆಯನ್ನು ಅಧಿಕೃತಗೊಳಿಸುತ್ತೇನೆ. ನನಗೆ ಅರ್ಥವಾಗುವ ಭಾಷೆಯಲ್ಲಿ ಹೇಳಲಾಗಿದೆ.

ಈ ಅಧ್ಯಯನದ ಉದ್ದೇಶ, ತಂತ್ರಜ್ಞಾನದ ಅಪಾಯಗಳು ಮತ್ತು ಪ್ರಯೋಜನಗಳು ಮತ್ತು ಅಧ್ಯಯನದ ಸಮಯದಲ್ಲಿ ಸಂಗ್ರಹಿಸಿದ ಮತ್ತು ಬಹಿರಂಗಪಡಿಸುವ ಮಾಹಿತಿಯ ಗೌಪ್ಯ ಸ್ವರೂಪವನ್ನು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ. ಸಂಗ್ರಹಿಸಿದ ಮಾಹಿತಿಯನ್ನು ಸಂಶೋಧನೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.

ಈ ಅಧ್ಯಯನದ ವಿವಿಧ ಅಂಶಗಳ ಬಗ್ಗೆ ಪ್ರಶ್ನೆಗಳನ್ನು ಕೇಳಲು ನನಗೆ ಅವಕಾಶವಿದೆ ಮತ್ತು ನನ್ನ ಪ್ರಶ್ನೆಗಳಿಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ.

ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಈ ಅಧ್ಯಯನದಿಂದ ಭಾಗವಹಿಸುವಿಕೆಯನ್ನು ಹಿಂಪಡೆಯಲು ನಾನು ಮುಕ್ತನಾಗಿರುತ್ತೇನೆ ಮತ್ತು ಇದು ಭವಿಷ್ಯದ ಕಾಳಜಿಯನ್ನು ಬದಲಾಯಿಸುವುದಿಲ್ಲ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವಿಕೆಯು ನನಗೆ ಯಾವುದೇ ಹೆಚ್ಚುವರಿ ವೆಚ್ಚವನ್ನು ಒಳಗೊಂಡಿರುವುದಿಲ್ಲ.

ಹೆಸರು	ಸಹಿ/ಹೆಬ್ಬೆಟ್ಟಿನಗುರುತು	ದಿನಾಂಕ	ಸಮಯ
ರೋಗಿಯ ಹೆಸರು			
ಸಾಕ್ಷಿಗಳ ಹೆಸರು			

ಪ್ರಾಥಮಿಕ ಸಂಶೋಧಕರು/ ವೈದ್ಯರು			

ANNEXURE-IV

PHOTOGRAPHS

PHOTOGRAPH 1 – SLIT LAMP EXAMINATION

PHOTOGRAPH 2: FUNDUS EXAMINATION BY 90 D LENS

PHOTOGRAPH 3: FUNDUS EXAMINATION BY IDO

PHOTOGRAPH 4: OCT EXAMINATION

ANNEXURE-V

KEY TO MASTER CHART

RE-Right Eye

LE – Left Eye

NPDR – Non-Proliferative Diabetic Retinopathy

PDR - Proliferative Diabetic Retinopathy

MASTER CHART

Serial no	UHID No	Age	Duration of Diabetes	Sex	HbA1c levels	RIGHT EYE (µm)			LEFT EYE (µm)			Cube volume (mm3)		Grade of retinopathy changes	
						CENTRAL	NASAL	TEMPORAL	CENTRAL	NASAL	TEMPORAL	RE	LE	RE	LE
1	902804	62	14	M	8.8	262	309	302	296	316	382	9.9	10.7	Moderate NPDR	Mod NPDR
2	902791	62	16	M	9.2	357	368	327	379	519	362	10.7	13.7	severe NPDR	PDR
3	800997	72	19	F	7.6	261	300	320	184	273	250	11	9.4	Moderate NPDR	Mod NPDR
4	902550	68	17	M	7.1	294	339	343	292	325	315	10.4	10.2	Moderate NPDR	severe NPDR
5	796662	72	20	M	6.9	158	233	244	192	256	272	7.4	9.6	NO DR	NO DR
6	814732	64	12	F	7.9	319	275	409	330	304	382	9.9	8.9	Moderate NPDR	NO DR
7	810219	68	14	M	6.7	205	278	302	173	256	338	10.1	9.9	Moderate NPDR	Mod NPDR
8	831297	74	21	M	7.9	240	292	268	256	323	313	9.4	10.1	NO DR	NO DR
9	846219	60	11	M	8.9	230	324	296	261	343	320	10	10.5	NO DR	NO DR
10	832489	61	11	F	7.6	222	267	287	224	293	272	9.9	9.7	Moderate NPDR	Mod NPDR
11	838612	63	13	M	7.7	250	315	293	244	203	245	9.2	9	Moderate NPDR	Mod NPDR
12	829614	75	25	M	7.2	252	276	296	229	302	264	9.8	13.6	NO DR	NO DR
13	819266	71	17	M	8.6	286	456	347	371	335	369	14.1	11.7	severe NPDR	severe NPDR
14	821578	62	13	M	7.1	250	297	297	244	287	289	9.6	9.9	NO DR	NO DR
15	921234	52	10	M	8.9	274	324	321	274	308	322	10	9.4	Moderate NPDR	severe NPDR
16	811214	73	22	M	11.8	240	260	180	231	278	271	7.7	8.6	Moderate NPDR	Mod NPDR
17	708596	63	13	F	8.1	262	338	330	99	141	138	10.6	7.2	NO DR	NO DR
18	902571	41	10	M	7.3	237	319	307	230	312	301	10.1	9.8	Moderate NPDR	Mod NPDR
19	806751	71	20	M	9.8	335	359	292	148	261	230	9.8	8.9	Moderate NPDR	Mod NPDR
20	799986	62	12	F	9.9	230	357	317	425	594	399	10.8	15.3	PDR	PDR
21	808396	66	14	M	10.8	327	356	341	338	362	356	12.6	13.3	severe NPDR	PDR
22	904583	68	13	F	7.6	289	326	302	324	367	343	10.6	11.2	Moderate NPDR	Mod NPDR
23	895679	58	11	M	8.8	314	358	337	289	318	310	9.9	10.3	Moderate NPDR	Mod NPDR
24	949332	64	17	F	6.3	235	256	243	243	268	254	7.6	7.3	NO DR	NO DR
25	953812	54	11	M	5.9	198	223	246	211	248	234	7.1	6.9	NO DR	NO DR
26	902387	54	10	M	10.8	284	361	346	114	341	360	10	10.7	Moderate NPDR	Mod NPDR
27	845932	62	19	M	6.8	221	311	300	229	290	306	10.1	9.8	NO DR	NO DR
28	949311	52	11	M	8.3	291	365	352	292	357	351	10.7	11.3	severe NPDR	Mod NPDR
29	949295	68	20	M	10.9	301	354	367	328	368	391	11.9	12.3	Moderate NPDR	Mod NPDR
30	903457	49	11	M	6.9	182	212	232	201	234	223	7.1	7	no DR	NO DR
31	901267	59	14	F	7.4	222	267	287	224	293	272	9.9	9.7	NO DR	Mod NPDR
32	919033	53	12	F	7.1	175	224	241	190	252	265	7.8	8.1	NO DR	no DR
33	919598	69	21	M	8.1	273	301	298	254	289	301	8	7.9	Moderate NPDR	Mod NPDR
34	949297	81	27	M	9.4	268	324	296	261	343	320	10	10.5	NO DR	NO DR
35	934765	62	14	M	10.6	284	361	346	114	341	360	10	10.7	Moderate NPDR	Mod NPDR
36	901292	58	12	F	6.9	158	233	244	192	256	272	7.4	9.6	Moderate NPDR	Mod NPDR
37	902925	64	15	M	10.9	319	275	409	330	304	382	9.9	8.9	Moderate NPDR	Mod NPDR
38	953902	68	16	F	6.7	205	278	302	173	256	338	10.1	9.9	NO DR	NO DR
39	895978	44	10	M	7.1	222	267	287	224	293	272	9.9	9.7	mild NPDR	mild NPDR
40	902789	52	11	M	8.2	291	365	352	292	357	351	10.7	11.3	severe NPDR	Mod NPDR
41	899045	57	15	M	7	222	267	287	214	273	272	9.9	9.7	NO DR	NO DR
42	900226	50	11	F	7.6	234	267	273	224	293	272	9.9	9.7	Moderate NPDR	Mod NPDR

43	901890	54	13	F	6.9	157	196	213	192	256	272	7.4	9.6	no DR	Mod NPDR
44	902398	49	10	F	5.5	165	198	224	156	184	201	7.2	7.6	NO DR	NO DR
45	901258	41	10	M	7.3	237	319	307	230	312	301	10.1	9.8	severe NPDR	severe NPDR
46	878903	71	21	M	9.8	335	359	292	148	261	230	9.8	8.9	Moderate NPDR	Mod NPDR
47	901386	56	11	M	10.4	284	361	346	114	341	360	10	10.7	Moderate NPDR	Mod NPDR
48	941890	65	18	M	8.9	262	309	302	296	316	382	9.9	10.7	Moderate NPDR	Mod NPDR
49	800912	53	11	F	7.6	222	267	287	224	293	272	9.9	9.7	NO DR	NO DR
50	943652	64	16	M	8	198	243	256	204	256	275	7.2	7.7	no DR	NO DR
51	811212	59	15	F	7.1	214	253	275	224	293	272	9.4	9.7	Moderate NPDR	Mod NPDR
52	902550	53	12	F	8.9	262	309	302	296	316	382	9.9	10.7	Moderate NPDR	Mod NPDR
53	811296	62	16	M	9.2	357	368	327	379	519	362	10.7	13.7	severe NPDR	PDR
54	812782	72	23	F	7.6	261	300	320	184	273	250	11	9.4	Moderate NPDR	Mod NPDR
55	810219	59	12	M	7.1	294	339	343	292	325	315	10.4	10.2	Moderate NPDR	severe NPDR
56	813864	51	11	M	6.9	158	233	244	192	256	272	7.4	9.6	NO DR	NO DR
57	839610	63	18	F	9.1	268	324	296	261	343	320	10	10.5	Moderate NPDR	Mod NPDR
58	938764	49	10	F	7.2	222	267	287	224	293	272	9.9	9.7	NO DR	NO DR
59	838612	62	16	M	12.1	291	354	389	314	365	394	11.9	12.1	severe NPDR	severe NPDR
60	840130	48	10	F	6.9	158	233	244	192	256	272	7.4	9.6	NO DR	NO DR
61	796666	79	25	F	8.6	274	324	321	268	308	322	10	9.4	Moderate NPDR	severe NPDR
62	798219	61	20	M	7.9	232	270	298	224	293	272	9.9	9.7	Moderate NPDR	Mod NPDR
63	903534	57	17	M	7.2	222	267	287	224	293	272	9.9	9.7	Moderate NPDR	Mod NPDR
64	903567	50	12	F	8.2	262	293	301	252	273	301	10.1	9.9	Moderate NPDR	Mod NPDR
65	792318	49	10	M	7.1	250	291	297	244	287	289	9.6	9.9	NO DR	NO DR
66	792345	52	11	M	8.9	274	324	321	268	308	322	10	9.4	Moderate NPDR	severe NPDR
67	806783	68	20	M	11.8	240	265	180	231	278	271	7.7	8.6	Moderate NPDR	Mod NPDR
68	792319	47	10	F	6.9	158	233	244	192	256	272	7.4	9.6	NO DR	NO DR
69	831235	61	19	M	8.7	286	456	347	371	335	369	14.1	11.7	Moderate NPDR	severe NPDR
70	831112	55	12	M	11.3	301	333	345	288	313	324	13.6	12.9	severe NPDR	severe NPDR
71	949051	57	14	F	6.1	201	228	245	192	216	234	7.6	7	NO DR	NO DR
72	792616	45	10	M	6.9	167	204	226	189	243	232	7.1	7.3	mild NPDR	mild NPDR
73	953812	63	17	F	8	236	314	292	218	258	239	9.4	8.8	NO DR	NO DR
74	902645	58	14	M	8.4	264	293	301	248	278	291	8.8	8.3	no DR	NO DR
75	845654	43	10	M	6.9	271	324	302	232	274	292	9.1	8.9	no DR	no DR
76	949423	59	15	F	6.1	198	223	234	205	232	228	8.1	7.9	no DR	NO DR
77	949765	40	10	M	9.1	300	360	345	323	383	368	12.1	11.1	Moderate NPDR	Mod NPDR
78	903452	57	17	M	9.8	323	357	416	297	336	365	11.4	10.9	Sev NPDR	Sev NPDR
79	786354	60	15	F	8.2	253	286	301	243	264	286	7.9	8	Moderate NPDR	Mod NPDR
80	857463	52	11	F	7.3	223	288	273	246	301	294	8.4	9.1	mod NPDR	mod NPDR
81	657493	59	17	M	7.7	214	257	276	226	253	276	8.1	8.6	no DR	NO DR