Dissertation on

"AN ANALYTICAL STUDY TO EVALUATE THE ASSOCIATION BETWEEN FUNDUS FLUORESCEIN ANGIOGRAPHIC CHANGES IN DIABETIC MACULOPATHY AND DYSLIPIDAEMIA"

Submitted in partial fulfillment of requirements of

MASTER OF SURGERY DEGREE

BRANCH – III – (OPHTHALMOLOGY)

GOVT. RAJAJI HOSPITAL, MADURAI MEDICAL COLLEGE

MADURAI- 20

THE TAMILNADU

Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI

2018

CERTIFICATE

This is to certify that this dissertation entitled **"AN ANALYTICAL STUDY TO EVALUATE THE ASSOCIATION BETWEEN FUNDUS FLUORESCEIN ANGIOGRAPHIC CHANGES IN DIABETIC MACULOPATHY AND DYSLIPIDAEMIA"** is a bonafide record of research work done by **Dr. SRUTHI.R.S,** Post Graduate Resident in Department of Ophthalmology, Madurai Medical College, Madurai.

She has submitted this in partial fulfillment of the regulations laid down by The Tamil Nadu Dr. M.G.R. Medical University, for the award of Master of Surgery Degree Branch III (Ophthalmology), under our guidance and supervision during the academic years 2015-2018.

Prof. Dr. S. V. CHANDRAKUMAR, M.S, D.O.

HOD and Professor of Ophthalmology,

GRH, Madurai Medical College,

Madurai.

Dr. D.MARUTHUPANDIAN. MS. FICS.

The Dean,

GRH, Madurai Medical College,

Madurai.

CERTIFICATE FROM GUIDE

This is to certify that this dissertation entitled **"AN ANALYTICAL STUDY TO EVALUATE THE ASSOCIATION BETWEEN FUNDUS FLUORESCEIN ANGIOGRAPHIC CHANGES IN DIABETIC MACULOPATHY AND DYSLIPIDAEMIA"** is a bonafide record of research work done by **Dr. SRUTHI.R.S,** Post Graduate Resident in Department of Ophthalmology, Madurai Medical College, Madurai.

Prof. Dr. S. V. CHANDRAKUMAR, M.S, DO.

HOD and Professor of Ophthalmology,

GRH, Madurai Medical College,

Madurai.

DECLARATION

I, **Dr. SRUTHI.R.S** hereby solemnly declare that, this dissertation titled **"AN ANALYTICAL STUDY TO EVALUATE THE ASSOCIATION BETWEEN FUNDUS FLUORESCEIN ANGIOGRAPHIC CHANGES IN DIABETIC MACULOPATHY AND DYSLIPIDAEMIA"** was done by me.

I also declare that this bonafide work / a part of this work was not submitted by me / anyone else, for any award, for Degree / Diploma to any other University / Board either in India / abroad. This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of Master of Surgery degree Branch -III (Ophthalmology) to be held in May 2018.

Place: Madurai (Dr. SRUTHI.R.S)

Date:

ACKNOWLEDGEMENT

I express my sincere thanks and gratitude to **Prof. Dr D.MARUTHUPANDIAN MS FICS,** The Dean, GRH and MMC Madurai for permitting me to conduct this study. I am extremely grateful to my Guide **Prof. Dr. S. V. CHANDRAKUMAR. MS. DO,** HOD**,** Professor of Ophthalmology, and **Dr K..KAVITHA. MS. DNB**, Associate Professor of Ophthalmology GRH, MMC, Madurai, for their valuable suggestions and guidance throughout the course of my study. I have great pleasure in thanking my beloved Co-Guide **Dr.N.PARVATHASUNDARI, MS. DO;** Assistant Professor and all the Assistant Professors of Ophthalmology department at Madurai Medical College, Madurai, for their constant source of cheer and encouragement throughout the study.

I express my sincere thanks to **Prof. Dr. SENTHIL MD,** Head of the department of Diabetology for their constant support, guidance, cooperation in this study.

I thank all my dear friends for their timely help and encouragement to do my study. I express my heartfelt love to my family for endless affection and support.

I thank the patients of our hospital for their extreme patience and cooperation without whom this project would have been a distant dream.

Above all, I thank **GOD ALMIGHTY**for all his blessings.

INDEX

ANNEXURES

PART ONE

INTRODUCTION:

The incidence of Type 2 Diabetes Mellitus is turning out to be a near epidemic in India, and so is its complications like Diabetic retinopathy. Many of these patients belong to productive socioeconomic age group. Therefore identifying the risk factors for Diabetic Macular Edema and keeping them under check is of paramount importance in saving the vision of Diabetics, reducing morbidity and thus reducing the economic burden due to blindness in our country.

Diabetic retinopathy (DR) is a leading cause of visual disability and blindness among Diabetics. It is a major microvascular complication of diabetes and is frequently accompanied by lipid exudation. Dyslipidemia leads to the development of hard exudates and Clinically Significant Macular Edema (CSME) which interferes with vision. The elevated lipid levels are associated with endothelial dysfunction plays an important role in the pathogenesis of Diabetic Retinopathy, especially in the breakdown of blood-retinal barrier. It's important to find an association between serum lipid profile with diabetic retinopathy and its severity.

It is estimated that diabetes mellitus affects 4 percent of the world's population, nearly half of whom have some degree of diabetic retinopathy at a

given time. Diabetic retinopathy is a very common, long-term, microvascular complication of Diabetes Mellitus and a leading cause of visual disability and preventable blindness. It is considered the hallmark of generalized microangiopathy occurring in a Diabetic. In India the prevalence of diabetic retinopathy in general population is 3.5%, and the prevalence of diabetic retinopathy in the population with diabetes was 18.0%. In a population-based study in South India, diabetic retinopathy was detected in 1.78% of the diabetic patients who were screened.

While risk factors for the development and progression of diabetic retinopathy are multifactorial, the duration of the disease and the age of the patient are said to be the strongest predictors. Other risk factors like hypertension, pregnancy, blood glucose level control and presence of nephropathy are shown to have a strong association. Dyslipidemia, microalbuminuria, Body Mass Index and smoking are some of the factors whose role as predictors of diabetic retinopathy is not well established.

Diabetic retinopathy is frequently accompanied by lipid exudation. Elevated serum lipid levels are associated with increased risk of retinal hard exudate in patients with diabetic retinopathy. Although retinal hard exudate usually goes in hand with diabetic macular edema, increasing amounts of

exudate appear to be independently associated with an increased risk of visual impairment. The elevated lipid levels are also associated with endothelial dysfunction, which appears to play an important role in the pathogenesis of diabetic retinopathy, particularly in relation to the breakdown of blood-retinal barrier.

The association between serum lipid levels and diabetic retinopathy has been investigated in few studies. Some studies show a positive relationship between serum cholesterol and low-density lipoprotein levels and retinal hard exudation. Other studies show serum triglyceride levels as being important in the progression of retinopathy. Certain other studies show no relationship between serum lipid levels and diabetic retinopathy.

The current study was undertaken to determine the association of serum lipid profile with diabetic retinopathy and its severity. The conflicting reports in the literature regarding the association between serum lipid levels and diabetic retinopathy and the paucity of studies relative to the existing case load, has warranted this study.

ANATOMY OF RETINA:

The retina is the innermost coat of the eye. It extends from the optic disc to the oraserrata. It can broadly be divided into two distinct regions:

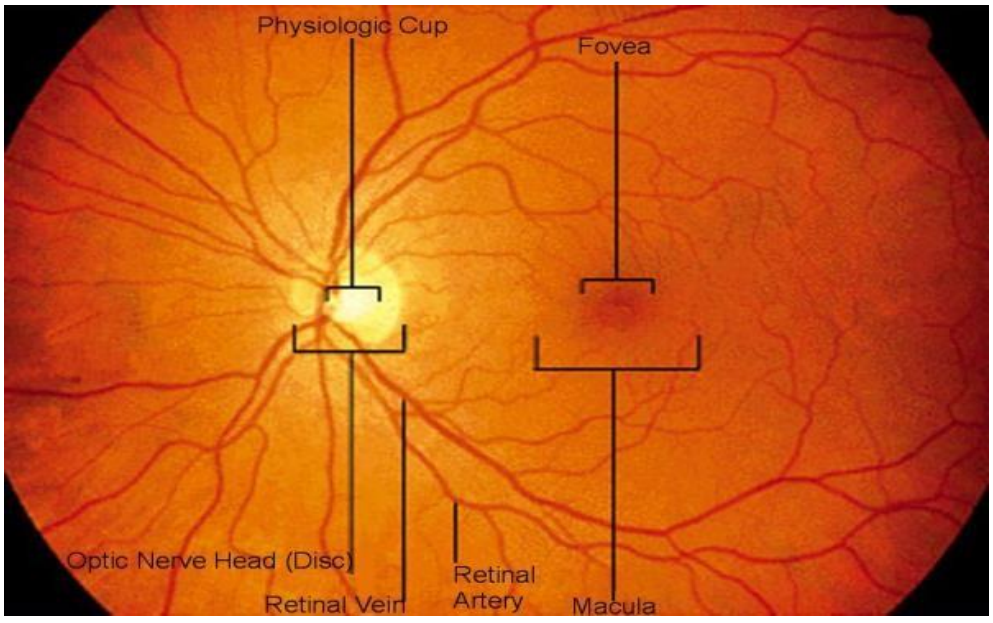
Posterior pole and **Peripheral retina** separated by the retinal equator. The *Retinal equator* is an imaginary line lying in line with the exit of the four vortex veins. The ***Posterior pole*** refers to the area of the retina posterior to the retinal equator. It includes two distinct areas: the optic disc and the macula lutea. Posterior pole of the retina is best examined by the slit-lamp Indirect Biomicroscopy using a +78D or +90D lens and direct ophthalmoscopy.

The Optic disc*:* It is a pink coloured, well-defined circular area of 1.5 mm diameter. At the optic disc all the retinal layers terminate except the nerve fibres, which pass through the lamina cribrosa to run into the optic nerve(second cranial nerve). A depression seen in the optic disc is called the *physiological cup*. The central retinal artery and the central retinal vein emerge through the centre of this cup.

The Macula: The macula lutea is also called the *yellow spot*. It is relatively deeper red than the surrounding retina and is situated at the posterior pole temporal to the optic disc. It is about 5.5 mm in diameter. The *Foveacentralis* is a central depressed part in the macula. It is about 1.5 mm in diameter and is the most sensitive part of retina. In its centre is a shining pit called *foveola*(0.35 mm diameter) which is situated about 2 disc diameters (3

mm) away from the temporal margin of the optic disc and about 1 mm below the horizontal meridian. An area of 0.8 mm size (which includes foveola and some surrounding area) does not contain any retinal capillaries and is called the FOVEAL AVASCULAR ZONE (FAZ). Surrounding the fovea are the parafoveal and perifoveal areas.

Peripheral retina refers to the area bounded posteriorly by the retinal equator and anteriorly by the oraserrata. Peripheral retina is best examined with indirect ophthalmoscopy or Goldman three mirror contact lens.



The retina contains at least 10 distinct layers. They are from outer to inner:

(1) the retinalpigment epithelium

(2) the layer of rods and cones (photoreceptor layer)

(3) the external limiting membrane

(4) the outer nuclear layer

(5) the outer plexiform layer

(6) the inner nuclear layer

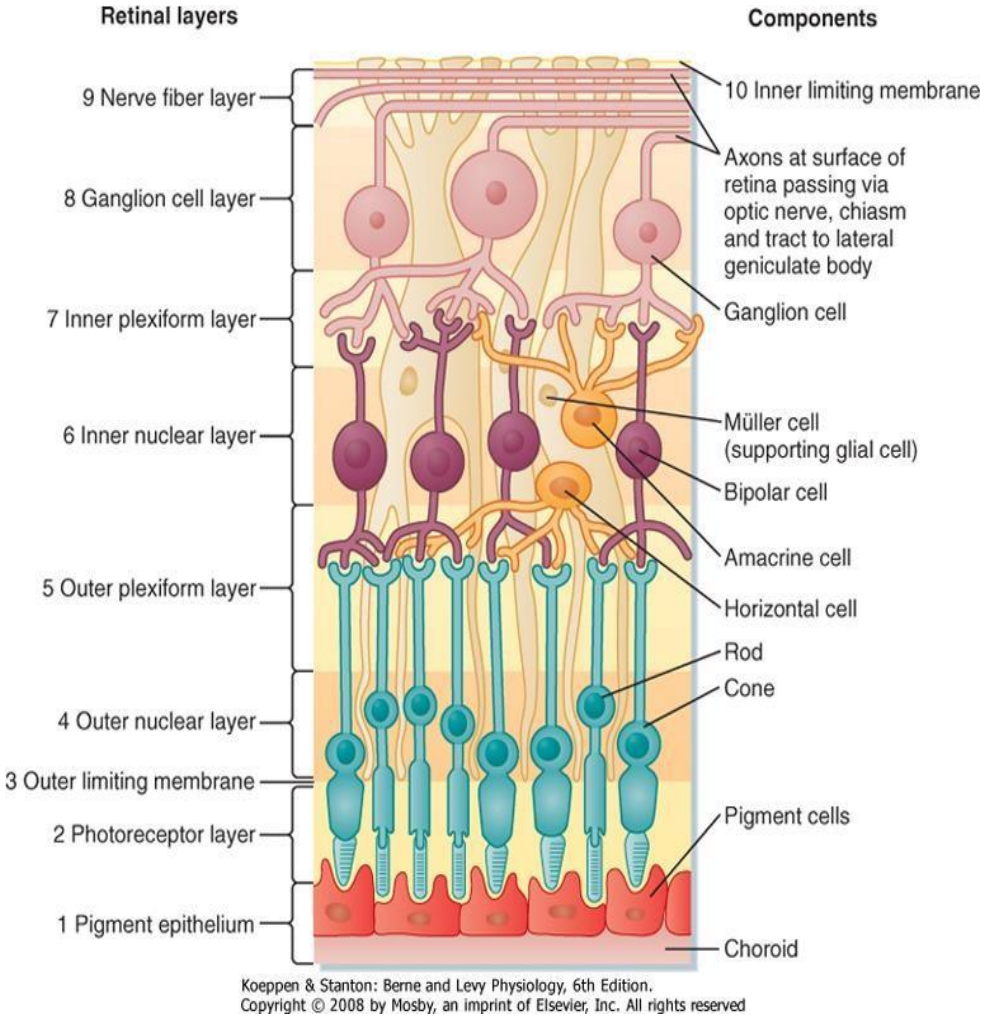
(contains the bipolar, amacrine and horizontal cells and nuclei of the fibres of Muller)

(7) the inner plexiform layer

(8) the ganglion cell layer

(9) the nerve fibre layer

(10) the internal limiting membrane



BLOOD SUPPLY OF THE RETINA:

The inner 6 layers of retina are supplied by the central retinal artery and the outer 4 layers are supplied by the choroidal artery.

The Arterial System:

The central retinal artery is a branch of the Ophthalmic artery which is inturn the first branch of the Internal carotid artery. The central retinal artery is an end artery. It enters the optic nerve approximately 1 cm behind the globe.

The artery wall has 3 anatomical layers:

- Intima: innermost layer which is composed of a single layer of endothelium resting on a collagenous zone.
- Internal elastic lamina: separates the intima from the media.
- Media: consists mainly of smooth muscle.
- Adventitia: is the outermost layer and is composed of loose connective tissue.

The **Retinal arterioles** arise from the central retinal artery. Their wall contains smooth muscle, but unlike the arteries, the internal elastic lamina is discontinuous.

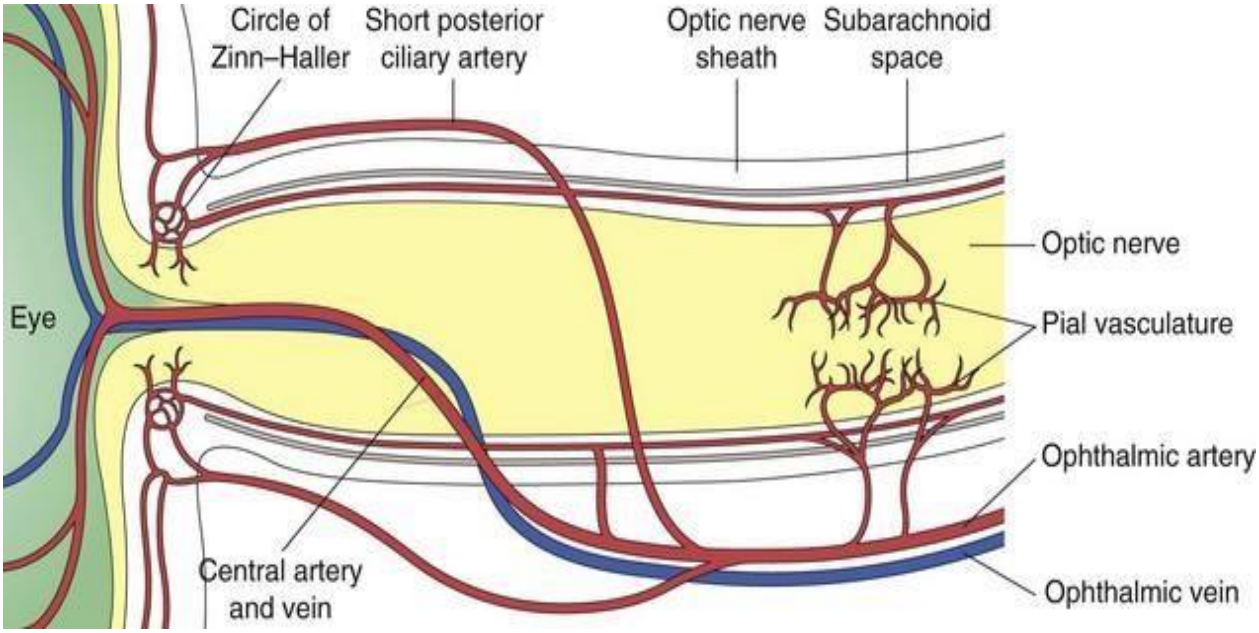
Retinal capillaries supply the inner two-thirds of the retina (inner 6 layers of retina), while the outer one-third(outer 4 layers of retina) are supplied by the choriocapillaris. The inner capillary network is located in the ganglion cell layer, and an outer capillary plexus lies in the inner nuclear layer. Capillary-free zones are present around arterioles and at the fovea (foveal avascular zone – FAZ).

The Retinal capillaries do not have smooth muscle and elastic tissue; and their walls consist of the following.

• The **Endothelial cells:** whichform a single layer on the basement membrane and are linked by tight junctions forming the inner blood–retinal barrier.

• The **basement membrane:** which lies beneath the endothelial cells with an outer basal lamina enclosing the pericytes.

• The **Pericytes:** which lie external to endothelial cells.They are supporting cells. They have many pseudopodial processes which envelop the capillaries. Pericytes have contractile properties and are thought to participate in the autoregulation of the microvascular circulation.



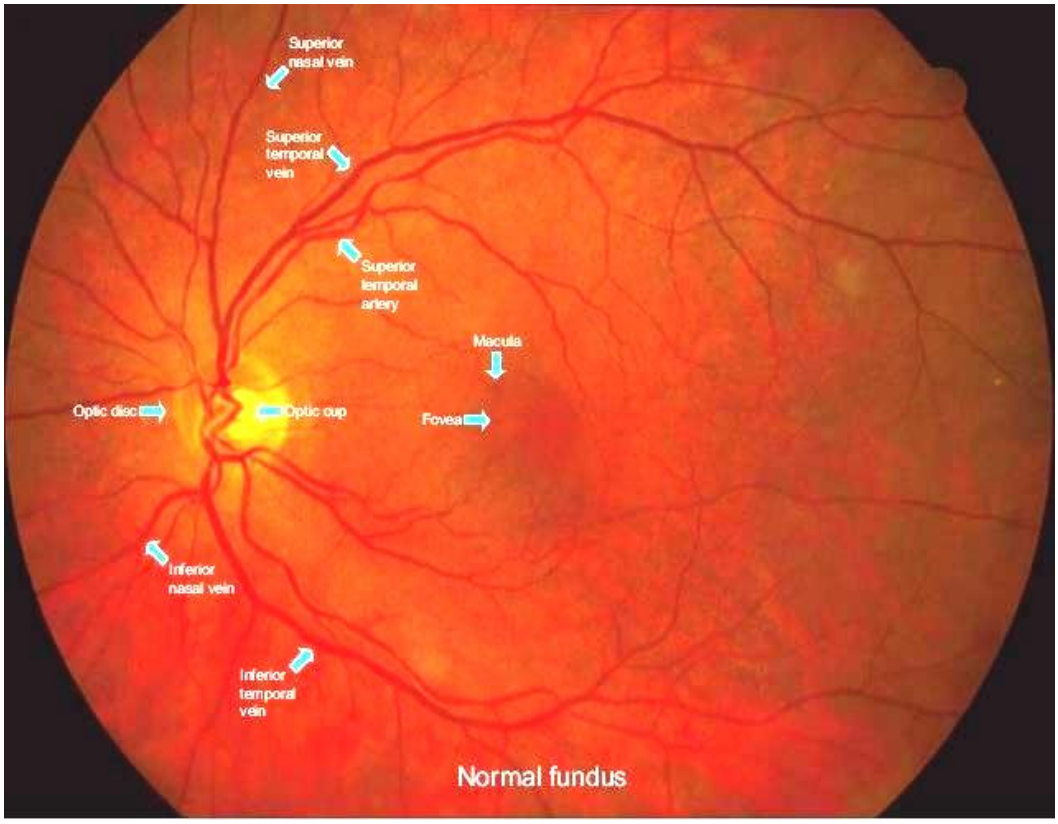
The Venous system:

Retinal venules and veins drain blood from the capillaries and finally drain into the Central Retinal vein.

• **Small venules** are larger than capillaries but have a similar structure.

• **Larger venules** contain smooth muscle and merge to form veins.

• **Veins** contain a small amount of smooth muscle and elastic tissue in their walls and are relatively distensible. Their diameter gradually enlarges as they pass posteriorly towards the central retinal vein.



DIABETIC RETINOPATHY:

Among the 422 million Diabetics in the world, India is among the top three countries with high diabetic population.

India has become the second biggest nation harbouring 64.5million diabetics next to China(102.9million diabetics).

Prevalence of Diabetic Retinopathy:

23 – 34% of patients of diabetes mellitus will have diabetic retinopathy

It is more common in type 1 diabetes than in type 2 diabetes and sight threatening disease is present in up to 10% diabetics. Proliferative diabetic retinopathy (PDR) affects about 10% of the diabetic population; type1 diabetics are at increased risk, with an incidence of up to 90%after 30 years.

Type 1 Diabetics are more prone to develop PDR leading to visual deterioration while the main cause of visual impairment is Type 2 Diabetics is Diabetic Macular edema.

DIABETES MELLITUS IN EYE:

Ophthalmic complications of diabetes mellitus include:

• **Common complications:**

○ Diabetic Retinopathy.

○ Diabetic Iridopathy (minor iris transillumination defects).

○ Refractive error.

• **Uncommon complications**

○ Recurrent hordeolum.

○ Xanthelasmata.

○ Accelerated senile cataract.

○ Neovascular glaucoma (NVG).

○ Ocular motor nerve palsy.

○ Reduced corneal sensitivity.

• **Rare complications:**

Diabetic Papillopathy, pupillary light-near dissociation, Wolfram syndrome (consists of progressive optic atrophy and multiple neurological and systemic abnormalities), acute-onset of senile cataract, rhino-orbital mucormycosis(fungal infection).

Risk factors

• **Duration of diabetes** is the most important risk factor. In patients diagnosed with diabetes before the age of 30 years, the incidence of Diabetic retinopathy after 10 years is 50%, and after 30 years 90%. DR seldom develops within 5 years of the onset of diabetes or before puberty, but about 5% of type 2 diabetics have DR at the time of presentation. Duration of diabetes is a stronger predictor for proliferative disease than for Diabetic maculopathy.

• **Poor control of diabetes.** It is proven that tight blood glucose control, when instituted early, can prevent or delay the development or progression of DR. Type 1 diabetics appear to obtain greater benefit from good control than type 2. Raised HbA1c level is associated with an increased risk of PDR.

• **Pregnancy** is said to be associated with rapid progression of DR. Predisposing factors include greater pre-pregnancy severity of retinopathy, poor pre-pregnancy control of diabetes(overt diabetes), control exerted too rapidly during the early stages of pregnancy and pre-eclampsia. The risk of progression is

directly related to the severity of DR in the first trimester. If substantial DR is present, frequency of review should reflect individual risk. Diabetic macular edema usually resolves spontaneously after pregnancy and need not be treated if it develops in later pregnancy.

• **Hypertension**, which is very common in patients with type 2 diabetes, should be rigorously controlled (<140/80 mmHg). Tight control can to be particularly beneficial in type 2 diabetics with maculopathy. Cardiovascular disease and previous stroke are also predictive factors.

• **Nephropathy**, if severe, is associated with worsening of DR. Hence, the treatment of renal disease (e.g. renal transplantation) may be associated with an improvement of retinopathy and a better response to photocoagulation.

• **Other risk factors** include hyperlipidaemia, smoking, previous cataract surgery, obesity and anemia.

Pathogenesis of Diabetic Retinopathy:

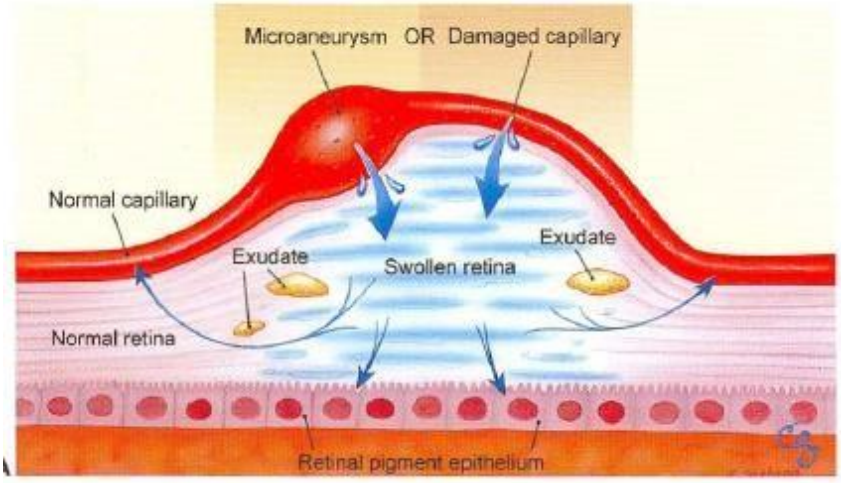
DR is predominantly a microangiopathy where small blood vessels are particularly susceptible to damage from high glucose levels. Direct hyperglycaemic effects on retinal cells also to play a role in causing DR. Many angiogenic stimulators and inhibitors have been found out; vascular endothelial growth factor (VEGF) seem to be of paramount importance in the former category.

Pathophysiology of DR:

Specific retinal capillary changes comprises the selective loss of pericytes and basement membrane thickening, which favor capillary occlusion and lead to retinal non perfusion, decompensation of the endothelial barrier function, which leads to serum leakage and retinal edema occurs.

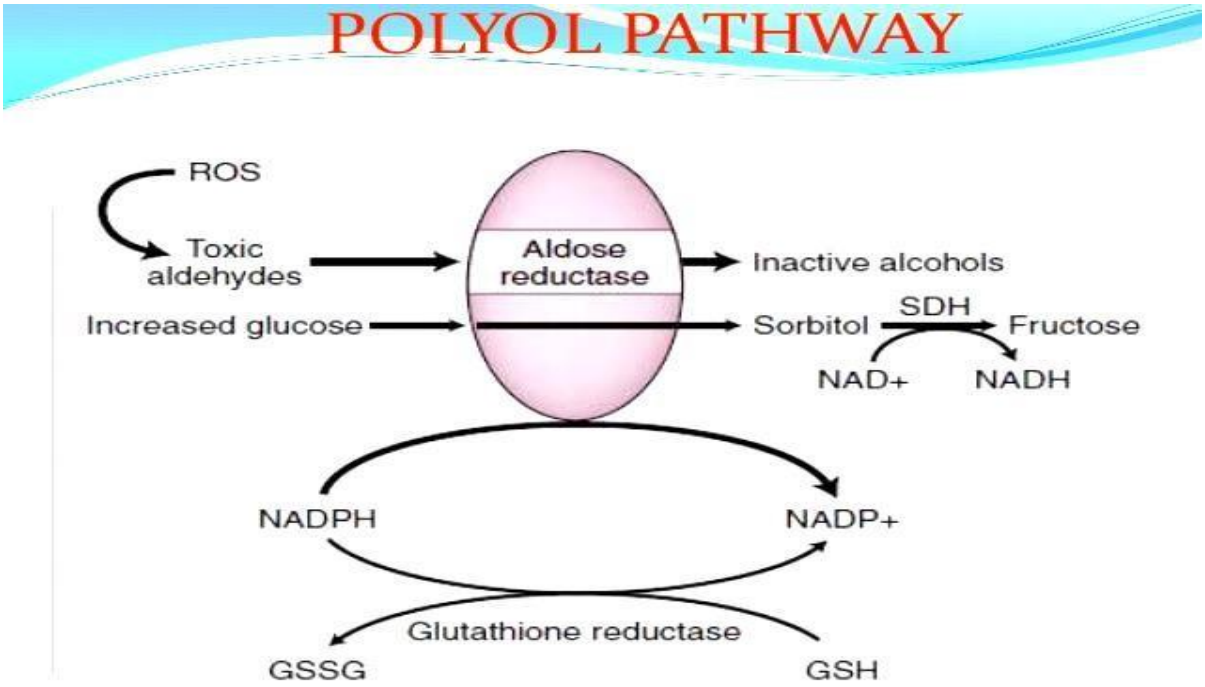
A variety of hematologic and biochemical abnormalities have been correlated with the prevalence and severity of Diabetic retinopathy:

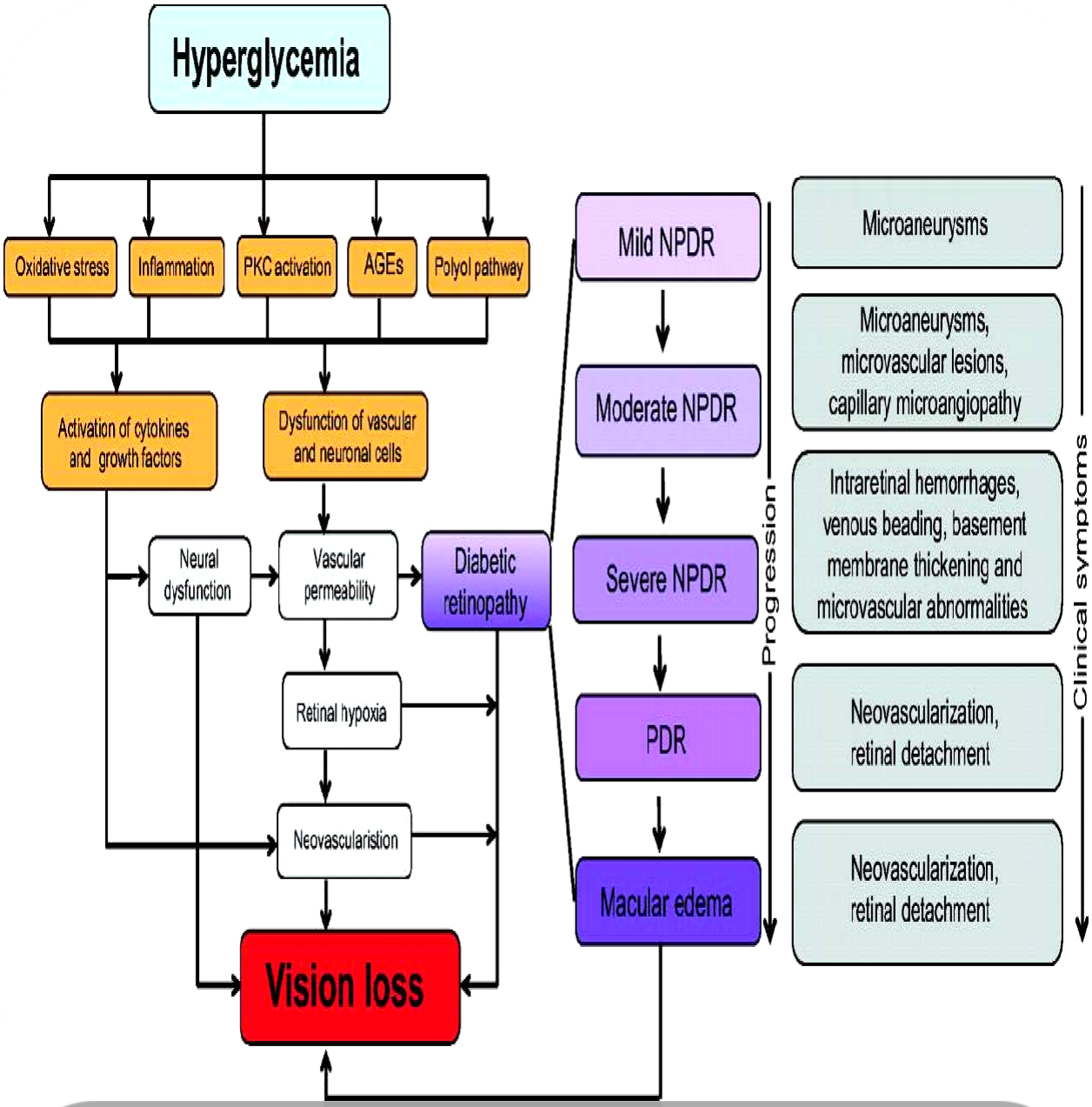
- increased platelet adhesiveness
- increased erythrocyte aggregation
- dyslipidemia
- defective fibrinolysis and increased fibrinogen
- abnormal growth hormone levels
- upregulation of vascular endothelial growth factor (VEGF)
- abnormalities in blood viscosity



Potential visual loss in diabetics with diabetic retinopathy may be due to the following:

- Diabetic macular edema (due to capillary leakage)
- macular ischemia (due to capillary occlusion)
- sequelae from ischemia-induced neovascularisation




Hyperglycemia
Oxidative stress
Inflammation
PKC activation
AGEs
Polyol pathway
Activation of cytokines and growth factors
Dysfunction of vascular and neuronal cells
Neural dysfunction
Vascular permeability
Diabetic retinopathy
Retinal hypoxia
Neovascularistion
Vision loss
Mild NPDR
Moderate NPDR
Severe NPDR
PDR
Macular edema
Progression
Microaneurysms
Microaneurysms, microvascular lesions, capillary microangiopathy
Intraretinal hemorrhages, venous beading, basement membrane thickening and microvascular abnormalities
Neovascularization, retinal detachment
Neovascularization, retinal detachment
Clinical symptoms

Pathological changes in DR:

1. Terminal arteriole :

Shows sclerotic changes, hyaline thickening (hyaline arteriosclerosis), corkscrew coiling, narrowed lumen and occlusion.

Venous side- 'U' shaped capillary loops, varicose dilatation.

2. Basement membrane – Thickened due to deposition of glycoproteins and layers are separated by debris and lipid droplets.

3. Pericytes loss - This leads to disruption of blood retinal barrier. (as pericyte maintains transport function and contractility)

Endothelial cell death may occur.

GHOST CAPILLARIES - occluded functionless vessels , basement membrane present but pericytes and endothelial cells are absent.

- Adjacent to ghost capillaries – distended tortuous shunt vessel develops to maintain the circulation.

4. Microaneurysm – Saccular or ampulliform shaped thin walled outpouchings and arise from side of capillaries near areas of capillary closure. In late stages – thickened and laminated due to PAS positive material deposition and they thrombose and lumen is occluded by laminated hyaline.

5 .Hemorrhage – most common in Outer plexiformlayer. Large hemorrhages may extend into the subhyaloid space

6. Exudates: in OPL – retina and Henle s layer – macula

7.Cotton wool spots – Infarct in NFL

8. NEW VESSEL : derived from venous side.

- Closely packed tufts , looping is clearly seen. After rupturing through ILM grows as pannus like network between retina and vitreous.
- They are fragile. Those which have attached to posterior face of retracting vitreous are liable to rupture and bleed.
- The mesenchyme from which the proliferating vessels are derived is a source of fibroblasts so that the vessels become enveloped in connective tissue which when contracts lead to Retinal Detachment.

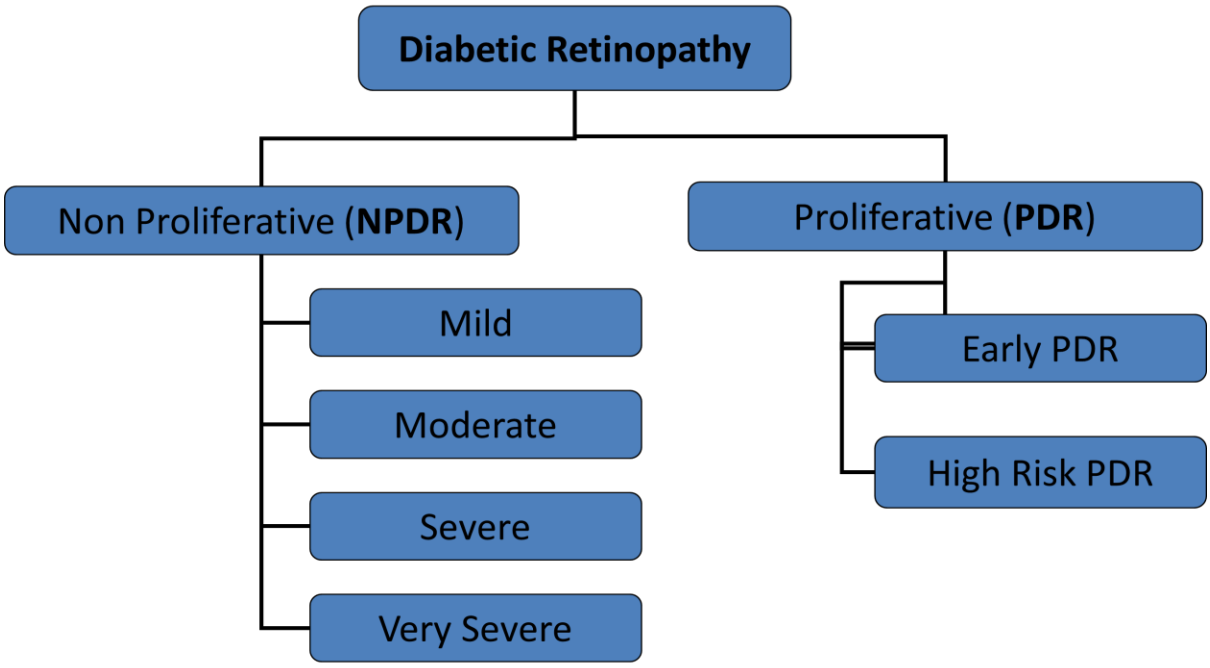
9. Degeneration of retinal nervous tissue:

- Both cells and dendrites of neurons – swollen and fragmented
- In late stages there is severe decrease in ganglion cells and NFL and gliosis of inner layers.

10. DIABETIC IRIDOPATHY :

- Vacuolation of pigment epithelium of iris due to accumulation of glycogen in epithelial cells .Retinal neovascularisation may be accompanied by growth of new vessels in iris leading to peripheral anterior adhesions and secondary angle closure glaucoma.

DIABETIC RETINOPATHY TYPES: NPDR AND PDR



1. Mild NPDR

- At least 1 microaneurysm or intraretinal hemorrhage.
- Hard/soft exudates may or may not be present.

2. Moderate NPDR

- Moderate microaneurysms or intraretinal hemorrhage.
- Early mild Intra retinal microvascular abnormalities (IRMA)
- Hard exudates or soft exudates may or may not present

3. *Severe NPDR.* Any one of the following (4-2-1 Rule):

- Four quadrants of severe microaneurysms or intraretinal hemorrhages.
- Two quadrants of venous beading.
- One quadrant of IRMA.

4. *Very severe NPDR.* Any two or more of the of the following (4-2-1 Rule)

- Four quadrants of severe microaneurysms or intraretinal hemorrhages.
- Two quadrants of venous beading.
- One quadrant of IRMA.

Retinal microvascular changes that occur in NPDR are limited to the retina and never extends beyond the internal limiting membrane (ILM). Characteristic findings in NPDR are microaneurysms, cotton-wool spots or soft exudates (boundary sentinels of infarction), areas of capillary nonperfusion, intraretinal microvascular abnormalities (IRMAs), “dot-and-blot” intraretinal hemorrhages, retinal edema, hard exudates, arteriolar abnormalities, and dilation and beading of retinal veins. NPDR can affect visual function through 2 mechanisms:

increased intraretinal vascular permeability, resulting in macular edema, and variable degrees of intraretinal capillary closure, resulting in macular ischemia.

PDR:

1. PDR without High Risk Characteristics (Early PDR).

2. PDR with High Risk Characteristics (Advanced PDR).

High risk characteristics (HRC) of PDR are the following:

- Neovascularisation Disc (NVD) 1/4 to 1/3 of disc area with or without vitreous haemorrhage (VH) or preretinal haemorrhage (PRH)
- NVD < 1/4 disc area with VH or PRH
- Neovascularisation Elsewhere (NVE)> 1/2 disc area with VH or PRH

CRITERIA FOR HIGH RISK PDR:

Any 1 of following:

- Mild Neovascularisation Disc (NVD) with vitreous haemorrhage
- Moderate to severe NVD with or without vitreous haemorrhage (¼ to 1/3 disc area of NVD)
- Moderate (1/2 disc area) Neovascularisation Elsewhere (NVE) with vitreous haemorrhage

Any 3 of the 4 retinopathy risk factors

- Presence of vitreous or preretinal hemorrhages
- Presence of new vessels
- Location of new vessels on or near the optic disc
- Moderate to severe extent of the new vessels

Advanced diabetic eye disease (ADED):

It is the ultimate end result of uncontrolled proliferative diabetic retinopathy. It leads to severe loss of vision. It is marked by the following complications;

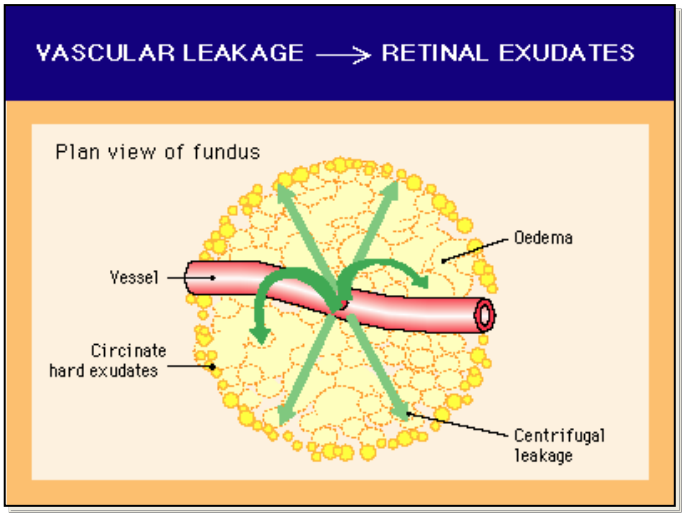
- Persistent vitreous haemorrhage
- Tractional retinal detachment
- Neovascular glaucoma.

Vision loss in patients with diabetic retinopathy are associated with the following abnormalities:

- capillary leakage (Diabetic macular edema)
- capillary occlusion (macular ischemia, diabetic papillopathy)
- sequelae from ischemia-induced neovascularization (vitreous hemorrhage, tractional retinal detachment, and neovascular glaucoma)

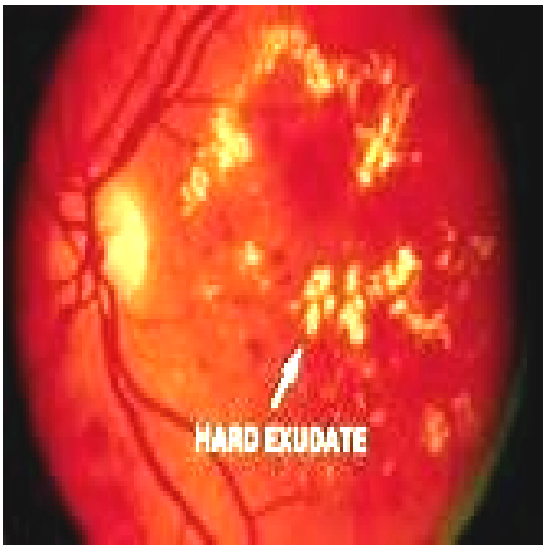
HARD EXUDATES

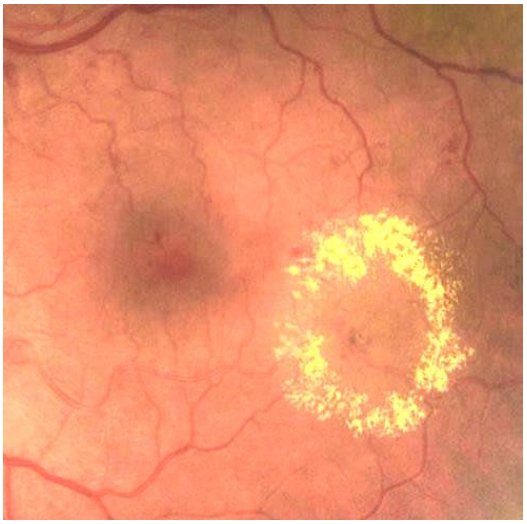
Hard exudates are morphological signs of blood retinal barrier breakdown. Biochemically, there are composted of lipoproteins of plasma origin. They are deposited in the inner and outer plexiform layers and are exuded from microaneurysms. Areas of hard exudates are surrounded by an accumulation of macrophages. When arranged in dense conglomerates, they may cause localized scotoma.



- Caused due to the break down lipid products of neuronal elements.
- Colour: They are discrete yellow material
- Location: Outer plexiform layer of the retina
- Appearance: Circinate arrangement seen around leaking MA/capillaries

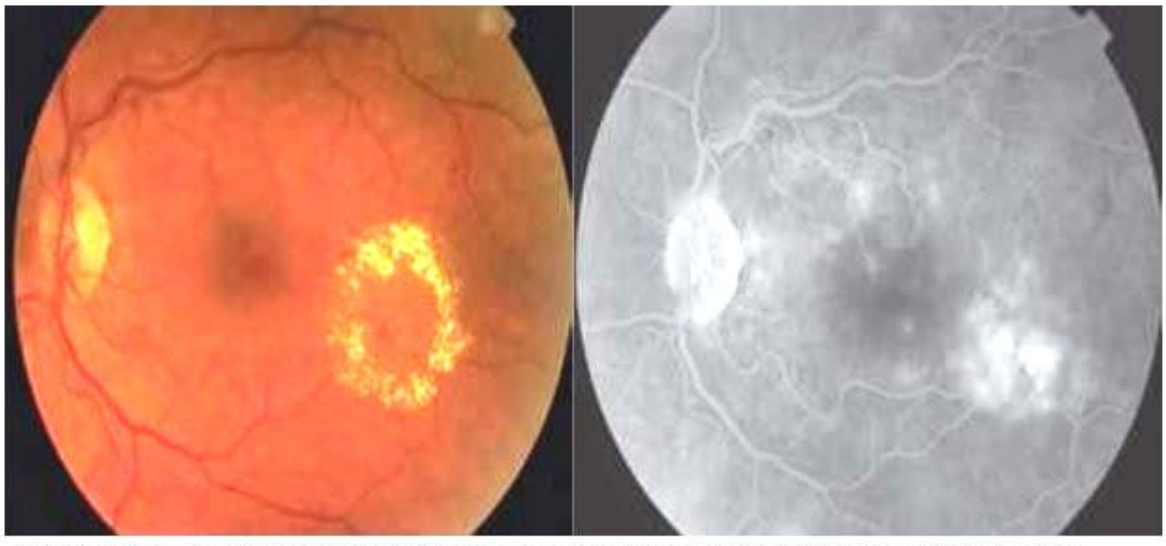
- Hard exudates indicate Abnormal vascular leakage
- They are removed by the phagocytic action of macrophages by 6 months to 12 months





.

HARD EXUDATE



HYPOFLUORESCENCE DUE TO BLOCKAGE OF BACKGROUND CHOROIDAL FLUORESCENCE

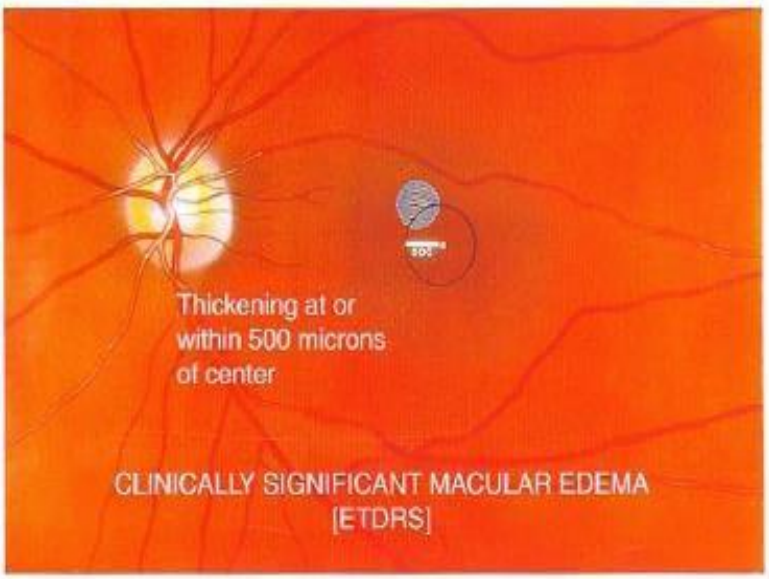
CLINICALLY SIGNIFICANT MACULAR EDEMA :

Clinically significant macular edema (CSME) is detected on clinical examination by ophthamoscopy, as defined in the ETDRS.

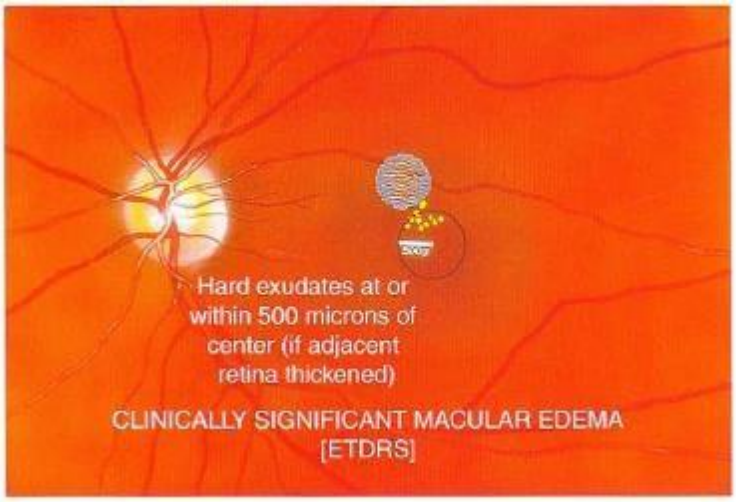
The Early Treatment Diabetic Retinopathy Study (ETDRS) was the first prospective, randomized clinical trial of photocoagulation in diabetic patients with less than high-risk PDR to establish standard treatment paradigms for managing DME.

CSME includes Any one of the following:

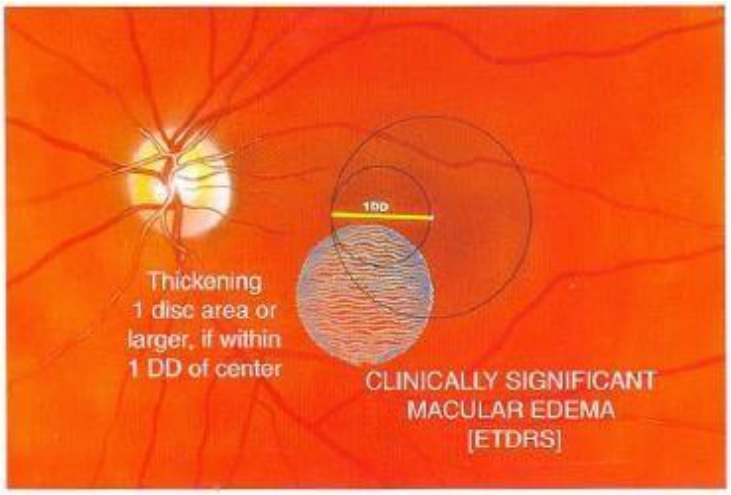
• Retinal thickening within 500 μm of the centre of the macula



• Exudates within 500 µm of the centre of the macula, if associated with retinal thickening; the thickening itself may be outside the 500 µm



• Retinal thickening one disc area (1500 µm) or larger, any part of which is within one disc diameter of the centre of the macula and demonstrates CMO if present.



Studies now use the term *center-involving macular edema* or similar terminology, based on whether or not the fovea appears thickened on OCT scans. Most algorithms for pharmacologic intervention use this simplified, OCT-based definition.

Early Treatment Diabetic Retinopathy Study (ETDRS):

The study aimed at the following Questions:

1. Is photocoagulation effective for treating Diabetic macular edema (DME)?
2. Is photocoagulation effective for treating diabetic retinopathy?
3. Is aspirin effective for preventing progression of diabetic retinopathy?

Eligibility: Mild nonproliferative diabetic retinopathy through early proliferative diabetic retinopathy, with visual acuity 20/200 (6/60) or better in each eye.

Randomization: 3711 participants: 1 eye randomly assigned to photocoagulation (scatter and/or focal) and 1 eye assigned to no photocoagulation; patients randomly assigned to 650 mg/day aspirin or placebo.

Outcome variables: Visual acuity less than 5/200 for at least 4 months; visual acuity worsening by doubling of initial visual angle (eg, 20/40 to 20/80); retinopathy progression.

Macular edema results:

1. Focal photocoagulation for DME decreased risk of moderate vision loss (doubling of initial visual angle).
2. Focal photocoagulation for DME increased chance of moderate vision gain (halving of initial visual angle).
3. Focal photocoagulation for DME reduced retinal thickening.

Early scatter photocoagulation results:

1. Early scatter photocoagulation resulted in a small reduction in the risk of severe vision loss (<5/200 for at least 4 months).
2. Early scatter photocoagulation is not indicated for eyes with mild to moderate diabetic retinopathy.
3. Early scatter photocoagulation may be most effective in patients with type 2 diabetes mellitus.

Aspirin use results:

1. Aspirin use did not alter progression of diabetic retinopathy.
2. Aspirin use did not increase risk of vitreous hemorrhage.
3. Aspirin use did not affect visual acuity.
4. Aspirin use reduced risk of cardiovascular morbidity and mortality.

DIABETIC MACULAR EDEMA:

Diabetic Maculopathy: Diabetes can affect macula in several ways, macular edema being the most frequent. It is also the most frequent cause of visual loss in the background stage.

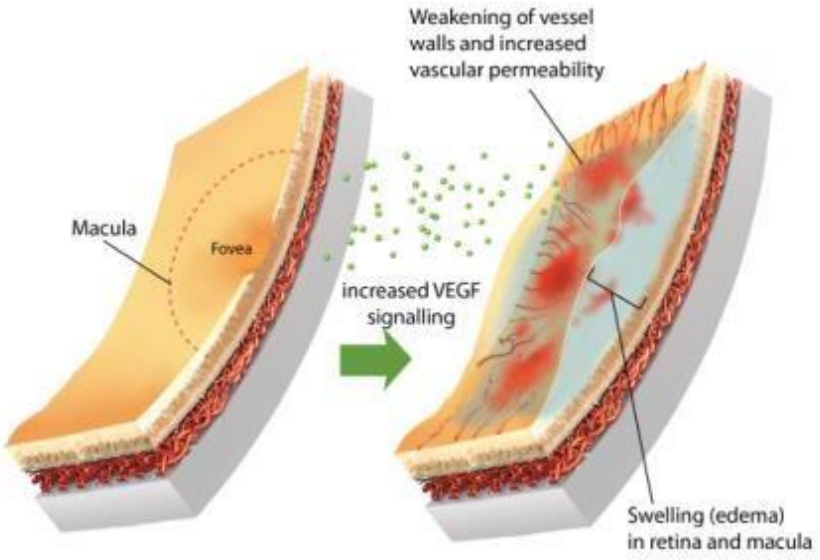
Diabetic Macular Edema is defined as a collection of interstitial fluid within the macula with or without lipid exudates and with or without cystoid changes. Clinically, macular edema is retinal thickening within two disc diameters of the center of the macular (not fluorescein leakage without thickening). Retinal thickening or hard exudates with adjacent retinal thickening that threatens or involves the center of the macular is considered to be clinically significant macular edema (CSME)

Macular edema may be Focal, Diffuse, Ischemic or a mixed variety.

It results mainly from breakdown of the inner blood retinal barrier. It may be present during any stage of retinopathy, though, the percentage of patients with macular oedema increases with increasing severity of retinopathy. Other factors influencing the development of macular edema are the age at onset of diabetes, type and the duration of diabetes. According to the Wisconsin Epidemiologic Study of Diabetic Retinopathy, “the prevalence rate of macular edema is 10% in the diabetic in the older onset patients and even in this group it is seen earlier

after the discovery of diabetes in the older onset patients and even in this group it is higher in those that are being treated with insulin (5% may already have macular edema at the time of diagnosis)"

Diabetic maculopathy (foveal edema, exudates or ischaemia) is the most common cause of visual impairment in diabetic patients, particularly in type 2 diabetics.. The fluid is initially located between the outer plexiform and inner nuclear layers; later it can eventually involve the inner plexiform and nerve fibre layers, until eventually the entire thickness of the retina becomes oedematous. The central accumulation of fluid the fovea forms a cystoid pattern named the cystoid macular edema (CME) that is readily detectable on optical coherence tomography (OCT) and assumes a central flower petal pattern on Fundus Fluorescein Angiography (FFA)



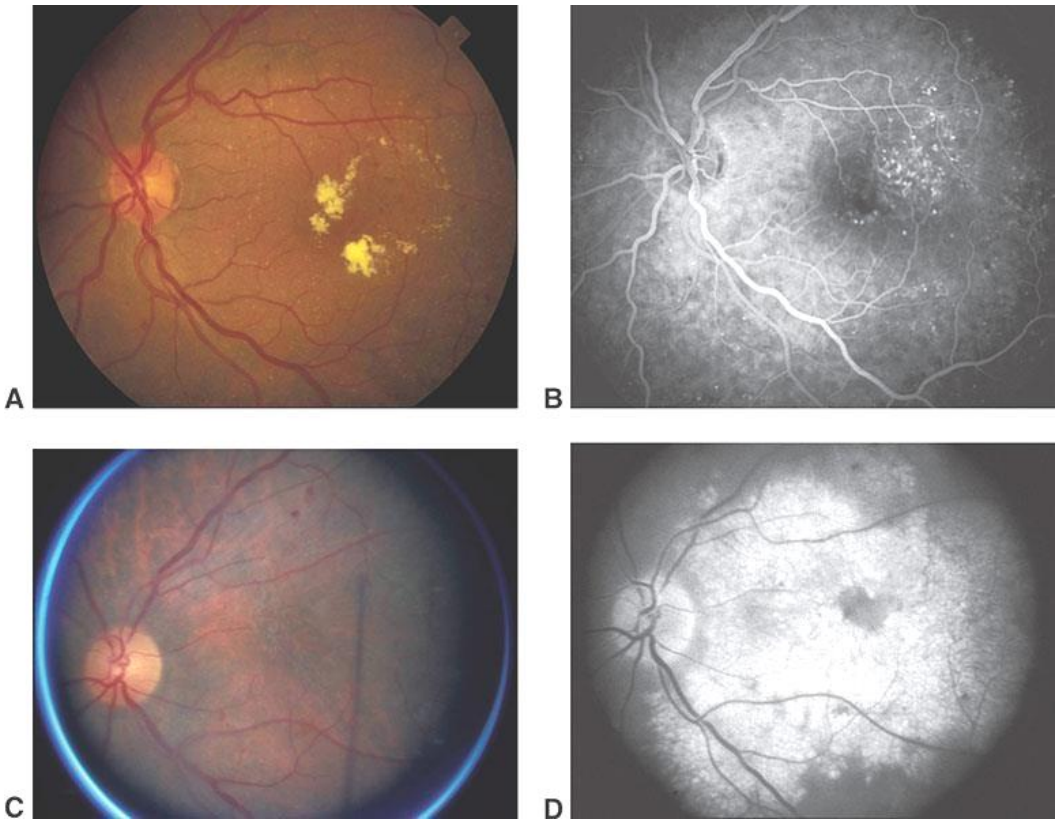
Types of Diabtic Macular Edema:

- **Focal maculopathy**: A well-circumscribed retinal thickening along with complete or incomplete rings of exudates FFA shows late, focal hyperfluorescence due to leakage from a microaneurysm and dilated capillary segments, usually with good macular perfusion.This is a localized leak from a microaneurysm giving rise to a hard exudate, deposited at the junction of normal and abnormal retina. Laser photocoagulation is often very successful in preventing or retarding visual loss and may even result in the visual improvement. However if the exudates are too far advanced, their resorption does occur following the laser treatment but retinal function may already have been destroyed due to which visual improvement may become impossible. Macular plaque is a long standing continued damage due to leakage into the macula.

• **Diffuse maculopathy**: There is diffuse retinal thickening, along with associated with cystoid changes; caused due to extensive capillary leak; there are typically scattered microaneurysms and small intraretinal haemorrhages . Landmarks may be obscured by edema, which may render localization of the fovea impossible. FFA shows mid- and late-

phase diffuse hyperfluorescence, It is characterized by a wide spread leakage of fluid from retinal capillaries, IRMAs &microaneurysms, leading to a diffuse macular oedema and a reduction in vision. Clinically, there is retinal thickening, loss of macular reflex and at a later stage development of cystoid macular edema due to a breakdown of the intervening normal retinal tissue. It may also present as scattered exudates in a non – circinate pattern. Without laser treatment in such cases, there is a continued fluid accumulation and destruction of the foveal architecture. Laser photocoagulation aims at limiting this destruction of macular structure and function.

Focal macular edema may be associated with hard exudates, which are precipitates of plasma lipoproteins. Because resorption of extravascular aqueous occurs at a faster rate than that of plasma lipids, lipid residues often remain behind after the fluid has resorbed. These yellow-to-white lipid deposits accumulate within the outer and inner plexiform layers or beneath the sensory retina.



Focal and diffuse macular edema.

A, Color fundus photograph showing circinate hard exudates surrounding a group of microaneurysms in an example of focal macular edema.

B, Fluorescein angiogram confirming the microaneurysms, which appear as a group of punctate foci of hyperfluorescence in FFA.

C, Color fundus photograph shows diffuse macular edema demonstrating diffuse thickening of the retina with glistening surface.

D, Fundus Fluorescein angiogram confirming the diffuse intraretinal leakage.

Diffuse macular edema is characterized by extensive retinal capillary leakage and widespread breakdown of the blood–retina barrier, often accumulating in a cystoid configuration in the perifoveal macula (cystoid macular edema)

Whether the pattern of macular edema is focal or diffuse, treatment decisions are based upon lesions meeting defined size and location criteria that determine clinical significance.

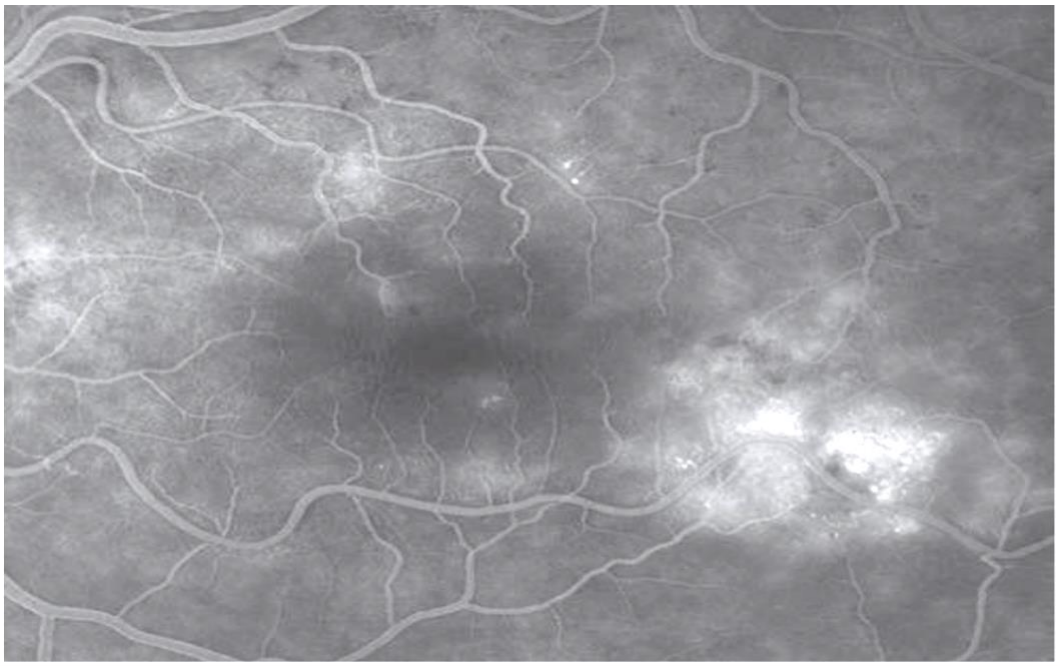
- ***Ischaemic maculopathy:***

This type of maculopathy occurs as a result of non-perfusion of the parafoveal capillaries with or without intraretinal fluid accumulation. It usually coexists with the other types, but in its pure form is the least easy to recognize and diagnose. Ophthalmoscopically one may find a dull appearance to the macula. However an FFA is necessary to confirm the diagnosis. It is essentially untreatable. Improvement of a poor diabetic control may retard the progression, but too rapid an implementation can also lead to a transient worsening of retinal ischemia. Prepoliferative and proliferative changes should be actively looked for in such cases and treated early because it will help reduce the risk of further visual loss from extra – macular complications. Microaneurysms may cluster at the margins of zones of capillary nonperfusion of retinal arterioles and can result in larger areas of nonperfusion and progressive ischemia. Evidence of enlargement of the foveal avascular zone greater than 1000microns in diameter generally leads to visual loss.

Signs are variable and the macula may look relatively normal in Ophtalmoscopy, despite reduced visual acuity. In other cases PDR may be present.

FFA shows capillary non-perfusion(CNP) at the fovea (an enlarged FAZ) along with other areas of capillary non-perfusion at the posterior pole and the periphery.

ISCHEMIC MACULOPATHY:



* **Mixed:** Diabetic maculopathies rarely exist isolated and most commonly have two or more of the components listed above. Management is the treatment of remediable elements after assessing their respective contributions by FFA.

Other mechanisms in which macula is affected in diabetes are as follows:

- Traction on the macula by a fibrous tissue proliferation causing a drag of the retinal tissue, surface wrinkling or detachment of the macula.
- Intraretinal or preretinal (subhyaloid) haemorrhage on the macula.
- Lamellar or full – thickness macular hole formation.
- Any combination of the preceding.

FUNDUS FLUORESCEIN ANGIOGRAPHY:

FFA is a serial study of the vascular pattern of the retina and the choroid at specific time intervals to establish, confirm the diagnosis, to aid treatment decision and assess response to treatment.

Usually Retinal capillaries are absent in two regions:

1. Foveal Avascular Zone (300-400micron).
2. A 1.5 mm strip adjoining oraserrata.

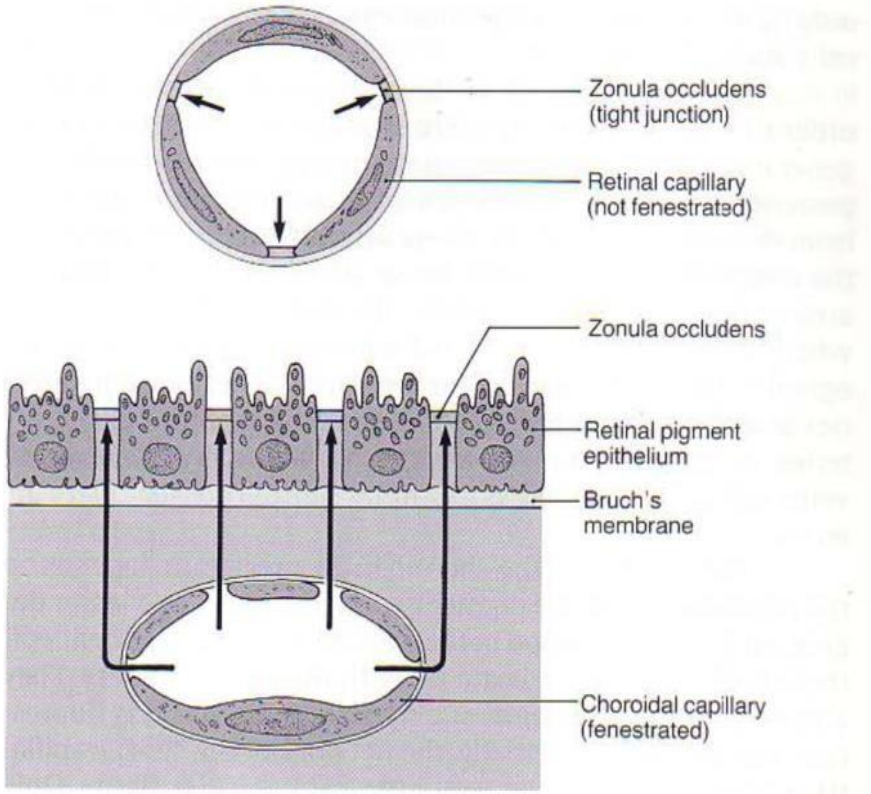
 The Inner blood retinal barrier: (walls of retinal vessels)

- Zonulae occludens.

- 1:1 endothelial andpericyte cell ratio.

- Outer blood retinal barrier:

  - retinal pigment epithelial tight junction.



Technique: Fluorescein Angiography requires the use of a fundus camera equipped with excitation and barrier filters. The Fluorescein dye(C20 H10 O5 Na2) is injected intravenously, usually through an antecubital vein with sufficient speed to produce high contrast images of the early phases of the

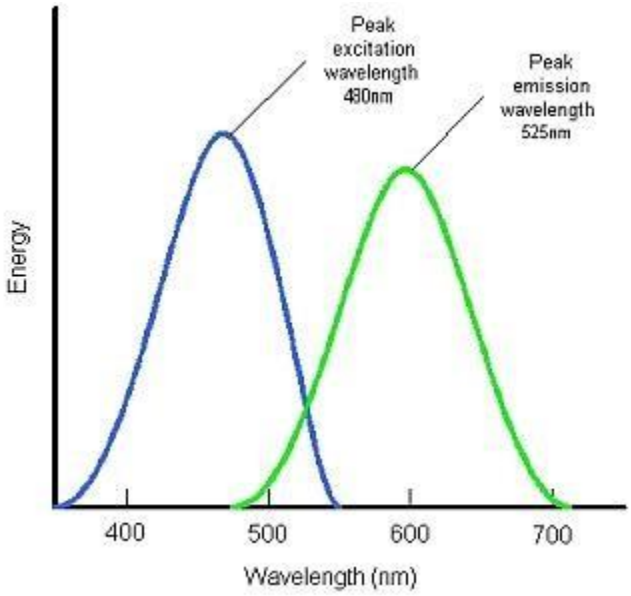
angiogram. 85% fluorescein is bound to serum proteins and 15% free unbound form in plasma.

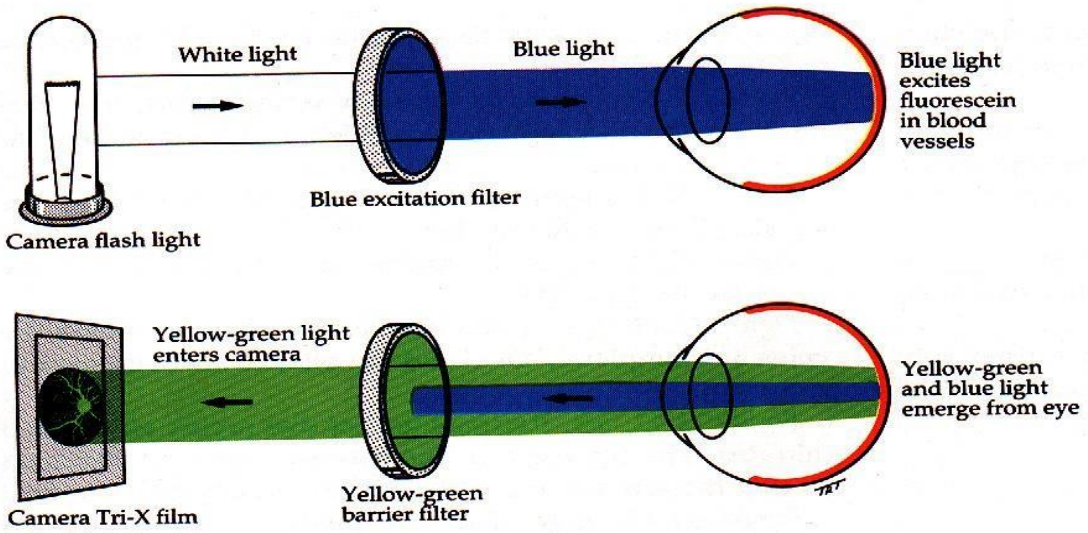
FUNDUS CAMERA

White light from a flash is passed through a blue excitation filter. Blue light (wavelength 465-490 nm) is then absorbed by the unbound fluorescein molecules, and the molecules fluoresce [emitting light with a longer wavelength in the yellow-green spectrum (520-530nm)]. A barrier filter blocks any reflected light so that the images capture only light emitted from the fluorescein. Images are acquired immediately after injection and continue for ten minutes depending on the pathology being imaged. The images are recorded digitally.

Preparations of sodium fluorescein available:

- 10 % Solution of 5 ml, 5% soln of 10ml(500mg).
- 25% Solution of 3 ml(750mg)





The Normal Fluorescein Angiography

Once Sodium Fluorescein dye is injected into the antecubital vein, the dye passes through the Ophthalmic artery and finally reaches the short posterior ciliary arteries and appears in the retina and choroid usually within 8-12 seconds. This is called the arm-retina time. This dependent on the age and cardiovascular status of the patient and the speed of dye injection.

The filling of the choroidal circulation is seen as the choroidal flush which in FFA appears as a patchy and mottled hyperfluorescence as the choroidal lobules fill. The dye appears in the retinal circulation1-3 seconds after it appears in the choroidal circulation (11-18 seconds after injection). This is followed by the early arteriovenous phase (AV phase)which describes the filling of the retinal arteries, arterioles and capillaries. Then comes the late arteriovenous phase or laminar venous phase as the Sodium fluorescein dye fills the veins in a laminar pattern.

In the normal macula, the capillary-free zone is seen as dark black area named the FAZ (Foveal Avascular Zone) due to blockage of choroidal fluorescence by Xanthophyll pigment and tightly packed retinal pigment epithelial cells in the macula. The peak phase with maximal fluorescence after dye injection occurs at about 30 seconds and then the recirculation phases follow. After 10 minutes fluorescein dye is not seen in retinal vessels at all however but structures like

the optic nerve head, Bruch's membrane, and sclera are stained with fluorescein and continue to fluoresce leading to delayed fluorescence.

Abnormal Fluorescein Angiography

Any Deviation from normal FFA is described as relative fluorescence. Hypofluorescence refers to a reduction from the normal expected fluorescence and hyperfluorescence refers to an increased fluorescence.

Hypofluorescence may occur due to a blocking effect or due to any vascular filling defect. Blockage of normal fluorescence can be due to any opacity anterior to the fluorescence hiding its view, like corneal scar, cataract, vitreous hemorrhage, and nerve fibre layer hemorrhage etc. Choroidal fluorescence may be blocked by retinal hemorrhage, subretinal precipitates, or even an abnormal collection of normal material in the retinal pigment epithelium as occurs with lipofuscins seen in Stargardt's disease. Vascular filling defect can cause an absence or delay in fluorescein dye entry in the tissue affected. Causes of vascular filling defects include retinal or choroidal vascular occlusion or with occlusion of the short posterior ciliary arteries supplying the optic nerve.

Hyperfluorescence can be due to fluorescein leakage, staining, pooling or by transmission defects and autofluorescence. Leaking fluorescein may come from incompetent blood vessels which leaks such as with

Choroidal neovascularization or diabetic neovascularization or though a diseased retinal pigment epithelium that no longer blocks leakage of fluorescein from the choroid. Areas of leakage in an FFA show gradual enlargement and blurring of their margins. This is different from staining of structures that stain. Staining results in increasing fluorescence throughout the angiogram but the margins remain well defined and distinct. Normal structures like the optic disc and sclera will stain. but pathological structures like drusen and disciform scars, also stain with sodium fluorescein. Pooling is caused when fluorescein gradually fills a fluid-filled space. A transmission, or window defect, is formed when a layer that normally blocks fluorescence is missing. This usually occurs when the retinal pigment epithelium is missing and the bright choroidal fluorescence is seen early in the FFA. The intensity of the fluorescence fades and the margins remains welldefined. Ocular structures such as optic nerve head drusen and lipofuscin normally fluoresce even before fluorescein dye injection and this is called Autofluorescence. Some authorities suggest that specifically equipped scanning laser ophthalmoscopes and fundus cameras can use the fluorescence of lipofuscin to document the health of the RPE layer instead of using sodium fluorescein dye.

Phases in FFA:

i. Prearterial phase

ii. Arterial phase

iii. Arterio venous phase

iv. Venous phase

v. Transit phase

vi. Recirculation phase

PREARTERIAL PHASE: The larger choroidal vessels and choriocapillaries begins to fill. Fluorescein is faint patchy irregularly scattered.

ARTERIAL PHASE: Dye fills the most choroidal vessels and also retinal vessels. Flourescein increases in intensity. Fast & turbulent circulation, hence no lamination.

ARTERO-VENOUS PHASE: Complete filling of arteries and capillaries.

First evidence of laminar flow in vein.

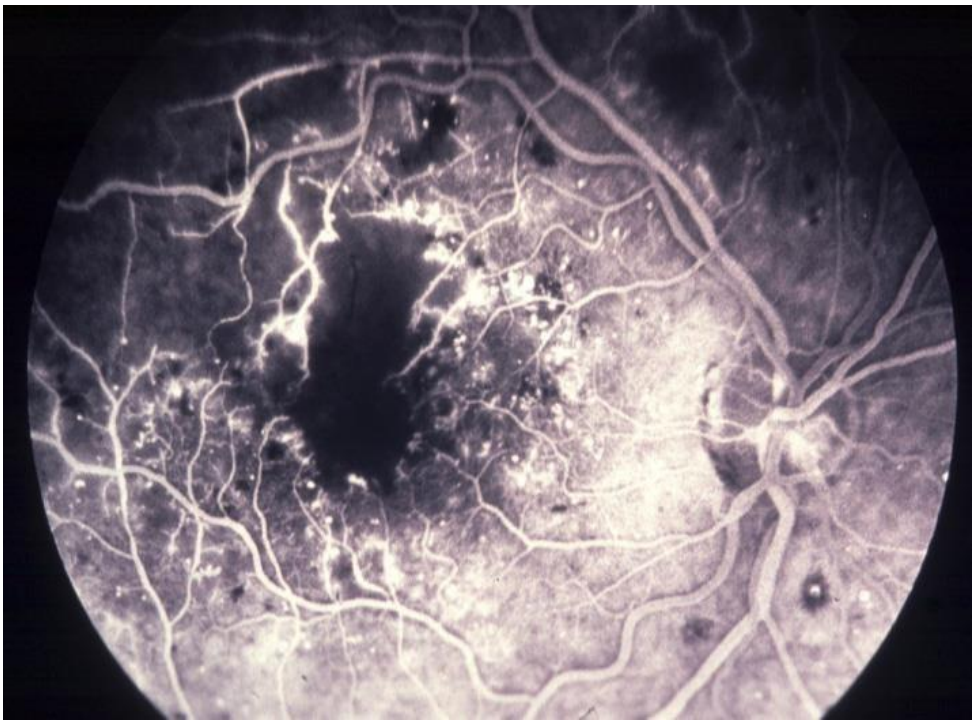
- Blood stream is faster in the centre of the lumen so unbound dye is appears to stick on the side creating laminar pattern.

VENOUS PHASE: Arteries begins to emptying and veins are completely filled. At the junction of two veins, the inner lamina of each vein merge and create third lamina. As dye filling increases, lamina enlarge and completely fills the vein.

TRANSIT PHASE: Includes the arterial, arterio-venous, venous phase. It represents the complete passage of fluorescein containing blood through the retina and choroid. FAZ is better identified.

RECIRCULATION PHASE: Fluorescein at low concentration continues to pass through fundus circulations. Vessels slowly empty the fluorescein and become gray. Staining of disc-normal.

FFA IN DIABETIC MACULAR ISCHEMIA:



Role of Fundus Fluorescein Angiography (FFA) in Diabetic Retinopathy:

Background Diabetic Retinopathy

- Baseline
- Maculopathy – unexplained visual loss

Clinically Significant Macular Edema

- Ischemia
- Extent

- Location

Preproliferative Diabetic Retinopathy

- Extent of retinal ischemia : Capillary non perfusion areas
- Detect NVE, NVD which are not clinically evident
- IRMAs
- Maculopathy

Proliferative Diabetic Retinopathy

- Confirm clinical findings
- Residual or recurrent proliferations after laser treatment

Background Diabetic Retinopathy

Regular clinical checkup is mandatory to look for the development of the following:

* Maculopathy
* Preproliferative changes
* New vessels on the disc elsewhere
* CSME

Focal laser treatment for CSME consists of direct laser treatment, grid laser treatment, or a combination of the two. Based on previously mentioned randomized clinical trials for treatment of diabetic macular edema, following guidelines are recommended.

* Eyes with macular edema that is not clinically significant should generally be watched without treatment.

* Eyes with CSME with center involvement should be considered for immediate laser treatment.

* Eyes with CSME without center involvement should also be considered for immediate laser treatment, if the visual acuity is good.

In general, the following lesions are considered treatable:

* Focal leaks of more than 500 microns from center of macula causing thickening of exudation.

* Focal leaks 300 – 500 microns from center of macula, if the treatment is not likely to destroy the remaining perifoveal capillary network.

* Ares of diffuse leakage not treated previously

* Avascular zones other than the normal foveal avascular zone, not previously treated.

Factors favoring treatment include the evidence of advancing edema and that the treatable lesions causing the edema are located more than 500 microns form the center of fovea.

Technique: Usually a FFA is done prior to deciding the treatable lesions. In the ETDRS protocol these treatable lesions were as follows:

1. Discrete points of retinal hyperfluorescence or focal leakage, which were 500 micron or more from the centre of the macula causing hard exudates and / or retinal thickening.
2. Focal leaks 300 – 500 microns from the centre of the macula thought to be causing retinal thickening and / or hard exudates.
3. Areas if diffuse leakage within the retina (IRMA or diffusely leaking capillary bed).
4. Thickened retinal avascular zones (except for normal FAZ).

The treatment techniques could be

(a) **Focal Photocoagulation** or

(b) Grid treatment

Focal Photocoagulation : spot size from 50 to 200 microns of 0.1 seconds duration can be used to directly treat all the focal fluorescein leaks, which could include the microaneurysms, IRMAs or short capillary segments. The goal of treatment is too obtain closure or obliteration of the leak. The end point is a whitening or darkening of the microaneurysms.

Grid Photocoagulation: This is applied to areas of thickened retina showing diffuse fluorescein leakage on FFA or capillary drop out. Burns of light intensity are placed in this area using 50 to 200 microns spots of 0.1 sec or 0.5 sec duration. Grid is not placed within 500 micron of center of the macula or within 500 micron of the disc margin as they may lead to central scotoma, but can be placed in the papillomacular bundle. Peripherally, it can be placed in all directions upto 2 disc diameter from the center of the macula, or to the border of the PRP treatment. The main aim of the grid treatment is to 'tickle' the retinal pigment epithelial cells and stimulate the retino-choroidal pump to hasten the absorption of fluid and not to the destroy the region.

Follow-up treatment: At 4 weeks after treatment the patients are reviewed. If some obvious treatable lesions are missed at the initial session, they are treated four months after the initial treatment confirming this with FFA.

Follow up should be done at 4 monthly intervals. The patients should be explained in details that laser treatment that this is done to prevent any further visual loss and cannot revert the already lost vision.

DYSLIPIDAEMIA IN DIABETICS:

Hyperglycemia can result in cell damage by the following pathways:

- polyol pathway,
- upregulation of hexosamine pathway,
- advanced glycation end product (AGE) with increased expression of AGE receptors
- activation of protein kinase C (PKC) isoforms.

However, the corelation between traditional lipid markers and Diabetic Retinopathy remains unclear. Of all the hyperglycemia associated pathways, the protein kinase C (PKC) and Advanced Glycation Endproduct(AGE) pathways interact with blood Lipids. Protein kinase C (PKC) is a family of 10 enzymes, in which the 1/2 isoform appears to be closely associated with the development of Diabetic Retinopathy. Hyperglycemia results in an increase in glucose flux through the glycolysis pathway, that increases the de novo

synthesis of Diacylglycerol (DAG), the main activator of PKC in physiology. Moreover, the accumulated long-chain Fatty Acids are immediately converted into DAG. The expression of the PKC 1/2 isoform is increased in patients with diabetes mellitus. As PKC is involved in numerous physiological pathways, its upregulation contributes to the pathogenesis of Diabetic Retinopathy in the form of differential synthesis of extracellular matrix (ECM) proteins and their remodeling, increased release of angiogenic factors, endothelial and leukocyte dysfunction resulting in capillary occlusion and leukostasis, and eventually changes in the blood flow to retina.

Advanced Glycation Endproducts(AGEs) are generated by nonenzymatic reaction between reducing sugars and lipoproteins. Advanced Glycation End products are formed at a slow and constant rate in the normal body starting at embryonic development and accumulated over time. However, the formation of AGE is markedly increased in diabetes due to the increased availability of glucose. In a highly oxidative environment like retina, the accumulation of lipid and modification of proteins will lead to an accumulation of lipoxidation end products (ALEs).

There are two kinds of AGEs related to the pathogenesis of DR:

Carboxy-ethyl-pyrrole and malon-di-aldehyde (MDA). Advanced GlycationEndproducts(AGE)s are important pathogenic mediators which can

lead to a lot complications in Diabetes. They are seen in the retinal vessels of diabetics, and their levels correlates with those in serum and with the severity of the Diabetic retinopathy. The interaction of AGEs with specific cell surface receptors has been postulated in the onset of Diabetic Retinopathy. The AGE receptors include RAGE, galectin-3, CD36, and macrophage scavenger receptor. It is believed that exposure to high levels of Advanced Glycation End products(AGE)s leads to renal and vascular complications. In a study done by Hammes *et al*., the retinal capillaries showed an increased expression of AGEs and loss of pericytes 26 weeks after the development of diabetes in rats. Treatment with an AGE inhibitor, aminoguanidine (pimagedine) hydrochloride, significantly reduced AGE accumulation and prevented the rapid development of microaneurysms, pericyte loss and acellular capillaries.

REVIEW OF LITERATURE:

1. **Association of serum lipids with diabetic retinopathy in urban South Indians— the Chennai Urban Rural Epidemiology Study (CURES) Eye Study—2**

   M. Rema, B. K. Srivastava, B. Anitha, R. Deepa and V. Mohan

Aim

To study the association of serum lipids with diabetic retinopathy (DR) in Type 2 diabetic subjects.

Methods

Type 2 diabetic subjects (*n* = 1736) were randomly selected from the Chennai Urban Rural Epidemiology Study (CURES), which was carried out on a representative population of Chennai in South India. DR was diagnosed by retinal colour photography and classified according to the Early Treatment Diabetic Retinopathy Study (ETDRS) grading system. Classification of lipid abnormalities was done according to the National Cholesterol Education Programme–Adult Treatment Panel III (NCEP–ATP III) Guidelines.

Results

The mean serum cholesterol ($P = 0.024$), serum triglycerides ($P = 0.017$)

and non-high-density lipoprotein (HDL)-cholesterol (P =0.025) concentrations were higher in subjects with DR compared with those without DR. Multiple logistic regression analysis revealed that after adjusting for age, gender, duration of diabetes, total cholesterol Standardised regression estimate (SRE) = 1.178, 95% confidence interval (CI) 1.042, 1.331,P = 0.014), non-HDL-cholesterol (SRE = 1.169, 95% CI 1.040, 1.313, P = 0.012) and serum triglycerides (SRE = 1.292, 95% CI 1.136, 1.467, P = 0.001) were associated with DR and non-HDL-cholesterol (SRE = 1.264, 95% CI 1.000, 1.592, P = 0.045) and lowdensity

lipoprotein (LDL)-cholesterol (SRE = 1.453, 95% CI 1.107, 1.896, P = 0.005) with diabetic macular oedema (DME). After adjusting for HbA 1c and

body mass index, only triglycerides maintained a significant association with DR (SRE = 1.137, 95% CI 1.000, 1.291, P = 0.007) and LDL-cholesterol with macular oedema (SRE = 1.358, 95% CI 1.034, 1.774, P = 0.026).

Conclusions

There is a significant association of serum triglycerides with DR and LDL-cholesterol with DME.

Diabet. Med. 23, 1029–1036 (2006)

2. **Study of glycated haemoglobin, lipid profile and uric acid levels in diabeticretinopathy**

P. Usha Kiran1, B. Srinivas2

1Assistant professor, G.S.L.Medical College, Rajahmundry-533294, A.P, India.2Deputy civil surgeon, Rangaraya Medical College, Kakinada-533003, A.P, India.

Abstract: Diabetic patients with and without complications show a difference in serum uric acid pattern in relation to duration of disease along with glycemic status, lipid derangements and complications associated with the disease. HbA1c studies were taken to know the blood sugar levels for the past 3 months to assess the glycemic control. Study of lipid profile is also taken to assess the micro vascular complications like Retinopathy in diabetic cases. Behaviour of uric acid levels may indicate the ongoingpatho physiology in diabetes in relation to glycemic control, onset and progression of complications such as retinopathy. The present study consists of 75 cases of chronic diabetes with retinopathy as a complication in the age of 45-75 years. The values are compared with the values of 50 apparently healthy non-diabetics which will fall on the same age group. All the subjects were from ophthalmology department of Govt. General Hospital, Kakinada and also from Nayana Eye Care Hospital, Kakinada.

Results: The Mean, SD Values of HbA1C were high in whole blood group of diabetic retinopathy cases, 8.903, +1.549 as compared to control group. The Mean, SD values of uric acid of diabetic retinopathy cases are 4.796, +0.944,

which doesn‟t show much difference with control group, It shows that poor glycemic control plays a major role on the onset and progression of diabetic retinopathy. In diabetic retinopathy statistically significant lipid profile changes observed. Serum uric acid level has not shown statistically significant changes in diabetic retinopathy. It shows that uric acid values have no significance.

3. Relationship of Serum HbA1c and Fasting Serum Lipids with Central Macular Thickness in Patients with Type 2 Diabetes Mellitus

Abstract

Background: Diabetic retinopathy, the most common retinal vascular disease, is the leading cause of new-blindness in adults during the third through sixth decades of life.

Purpose: To determine the correlation between central macular thickness (CMT) and both HbA1c and fasting serum lipids level in early stage non proliferative diabetic retinopathy.

Results: The patients were divided into two groups as HbA1c >8.67% (Group I, n: 60) and HbA1c ≤8.67% (Group II, n: 72). The mean CMT of better eyes was 273.28±34.61 μm. The mean CMT of worse eye was 304.40±64.31 μm. According to comparison between Group I (HbA1c

>8.67%) and Group II (HbA1c ≤8.67%) the mean CMT's were not different in two groups (P: 0.37).

Main findings: HbA1c level (8.76%) were significantly higher than normal upper limits in patient even under diabetic medication. In further analyses the mean CMT's was not different in worse eye in Group I and Group II and it was not significantly different in better eyes in these two group either.

Conclusion: Even we did not observed any correlation between level of HbA1c and the degree of CMT statistically in either worse or better eye, result of our study showed that patient had increased macular thickness even early stage of NPDR while having significantly higher HbA1c even under systemic medication.

Brief Summary: The purpose of the current study was to determine the correlation between diabetic macular edema and both HbA1c and fasting serum lipids in early stage non proliferative diabetic retinopathy. We did not observed any correlation between level of HbA1c and the degree of central macular thickness (CMT) statistically in either worse or better eye. Our results may indirectly evidence of insufficient metabolic treatment can cause macular edema prior to other retinal signs.

4. Oxidized Low-Density Lipoprotein and the Incidence of Proliferative Diabetic Retinopathy and Clinically Significant Macular Edema Determined From Fundus Photographs

Ronald Klein, MD, MPH; Chelsea E. Myers, MStat; Kristine E. Lee, MS; Andrew D. Paterson, MBChB;
Karen J. Cruickshanks, PhD; Michael Y. Tsai, PhD; Ronald E. Gangnon, PhD; Barbara E. K. Klein, MD, MPH

IMPORTANCE Studies have shown oxidized low-density lipoprotein to be associated with the incidence of proliferative retinopathy and other complications of type 1 diabetes mellitus. Because low-risk interventions are available to modify oxidized low-density lipoprotein, it is important to examine the relationships between this factor and the incidence of proliferative retinopathy and of macular edema, 2 important causes of visual impairment in people with type 1 diabetes.

OBJECTIVE: To determine the association of oxidized low-density lipoprotein with the worsening of diabetic retinopathy and the incidence of proliferative retinopathy and of macular edema.

DESIGN, SETTING, AND PARTICIPANTS Of 996 participants with type 1 diabetes in the Wisconsin Epidemiologic Study of Diabetic Retinopathy, 730 were examined up to 4 times

(1990-1992, 1994-1996, 2005-2007, and 2012-2014) over 24 years and had assays of oxidized low-density lipoprotein and fundus photographs gradable for diabetic retinopathy and macular edema. Analyses started July 2014 and ended February 2015.

MAIN OUTCOMES AND MEASURES Worsening of diabetic retinopathy, incidence of proliferative diabetic retinopathy, and incidence of macular edema as assessed via grading of color stereo film fundus photographs. The levels of oxidized low-density lipoprotein collected from serum samples at the time of each examination were measured in 2013 and 2014 from frozen serum.

RESULTS The cohort at baseline had a mean (SD) level of oxidized low-density lipoprotein of30.0 (8.5) U/L. While adjusting for duration of diabetes, glycated hemoglobin A1c level, and other factors, we found that neither the level of oxidized low-density lipoprotein at the beginning of a period nor the change in it over a certain period was associated with the incidence of proliferative diabetic retinopathy (hazard ratio [HR], 1.11 [95%CI, 0.91-1.35],*P* = .30; odds ratio [OR], 1.77 [95%CI, 0.99-3.17], *P* = .06), the incidence of macular edema(HR, 1.04 [95%CI, 0.83-1.29], *P* = .74; OR, 1.08 [95%CI, 0.44-2.61], *P* = .87), or theworsening of diabetic retinopathy (HR, 0.94 [95%CI, 0.83-1.07], *P* = .34; OR, 1.32 [95%CI,0.83-2.09], *P* = .24).

CONCLUSIONS AND RELEVANCE Our findings do not provide evidence for a relationship between increasing levels of serum oxidized low-density lipoprotein and the incidence of macular edema or the worsening of diabetic

retinopathy in persons with type 1 diabetes. The potential increase in the HR for incident proliferative retinopathy, with an increase in oxidized low-density lipoprotein level over the preceding period, warrants further investigation of this relationship.

PART TWO

AIMS AND OBJECTIVES:

- To study the relationship between fundus fluorescein angiographic patterns of diabetic maculopathy and serum lipid levels.

- To evaluate the relationship between serum lipid levels and retinal hard exudates in patients with diabetic retinopathy.

STUDY PERIOD: 6months (April-October 2017)

SAMPLE SIZE: 50 patients.

ETHICAL CLEARANCE: Ethical Committee approval letter obtained

FINANCIAL SUPPORT: Nil

METHODOLOGY:

A total of 50 patients with diabetic retinopathy attending the O.P.D of the Department of Ophthalmology of Government Rajaji Hospital Madurai for ophthalmic evaluation detected to have diabetic maculopathy, who satisfy the inclusion criteria will be included in this study.

INCLUSION CRITERIA:

All patients of age > 21 years, with a confirmed diagnosis of Diabetic Maculopathy diagnosed with slit lamp biomicroscopy with 90D lens, or clinically and/or angiographically confirmed Diabetic Macular Edema. (Diabetes mellitus diagnosed on the basis of the diabetes diagnostic criteria of the World Health Organization, and the patients were under medical treatment by an experienced Diabetologist)

EXCLUSION CRITERIA:

1. Eyes with active proliferative retinopathy with vitreous haemorrhage and dense media opacities
2. Macular Edema due to causes other than Diabetis.
3. Very old uncompliant and Immunocompromised patients.
4. Patients who underwent Panretinal photocoagulation or anti-VEGF treatment
5. Gestational Diabetis.
6. Those with hypersensitivity to fluorescein dye or any other medications.
7. Patients with renal insufficiency, cardiovascular diseases.
8. Patients on hypolipidemic drugs and known case of Hyperlipidaemia Syndrome.

Subjects shall be evaluated for entry into the study and seen that they fulfill all eligibility criteria, and none of the exclusion criteria, will be invited to participate in the study. Written informed consent obtained from all of them.

METHOD OF COLLECTION OF DATA:

Patients with Diabetic Maculopathy attending OPD of the department of Ophthalmology of GovtRajaji Hospital, Madurai.

Informed consent will be taken.

A detailed history including demographics, ocular disease, past medical illness, drug history and personal history will be taken.

Ophthalmological examination will include:

Best corrected visual acuity assessed using illuminated Snellens chart.

Near vision assessed with Times New Roman chart.

Colour vision will be tested (monocularly) with Ishihara test plates.

Slit lamp examination for anterior segment especially lenticular opacities

Applanation tonometry

Refraction by retinoscopy

Amslers grid assessment for macular involvement.

Fundus examination with direct, indirect ophthalmoscope and slit lamp biomicroscopy 90 D lens for grading of diabetic retinopathy and macular assessment.

Fundus photograph will be taken before fundus flourescein angioigraphy.

Investigations like complete hemogram, urine examination, Biochemical tests- FBS, PPBS, HBA1C, **lipid profile**, serum creatinine will be recorded and ECG will be done. Medical fitness for performing the procedure will be taken. Patient will be explained about the procedure and proper written consent will be taken. Pupil will be dilated using tropicamide and phenylephrine for 20 to 30 min before the procedure. Emergency medicines will be kept available if needed and the test is performed in the presence of an Anaesthetist.

Fundus flourescein angiography will be done as follows:

Patient will be explained about the procedure. Patient will be seated and flourescein injected intravenously (after a test dose) followed by fundus photographs taken serially through dilated pupil for each eye separately. From the good quality fundus photographs, presence of leakage of perifoveal area will be recorded for both early and late frames separately. The presence of macular edema will be evaluated by comparing early-phase and late (5minute) phase frames for the presence of late phase leakage in the perifoveal area. Any enlargement of perifoveal avascular zone in late frames will be evaluated for ischemic maculopathy. These findings will be recorded separately. All poor quality FFA photographs will be excluded. . Following the procedure patient will be informed regarding urine and skin discolouration.

RESULTS AND INTERPRETATION

STATISTICAL METHOD:

The information collected regarding all the cases were recorded in a Master Chart.

Data analysis was done with the help of computer using Statistical Package for Social Sciences (SPSS) software developed by IBM corporation.

Using this software- range, frequencies, percentages, and‘p’ values were calculated.

“Chi Square” test was used to find the association btw lipid profile and FFA findings

A 'p' value of less than 0.05 is taken to denote significant relation

OBSERVATIONAL ANALYSIS

Table 1: AGE DISTRIBUTION

Age distribution of the group varied from 30-80 years. They were categorised into 5 classes with a class interval of 10years each. Majority of Diabetics developed Diabetic Maculopathy between the range of 50-60 years of age.

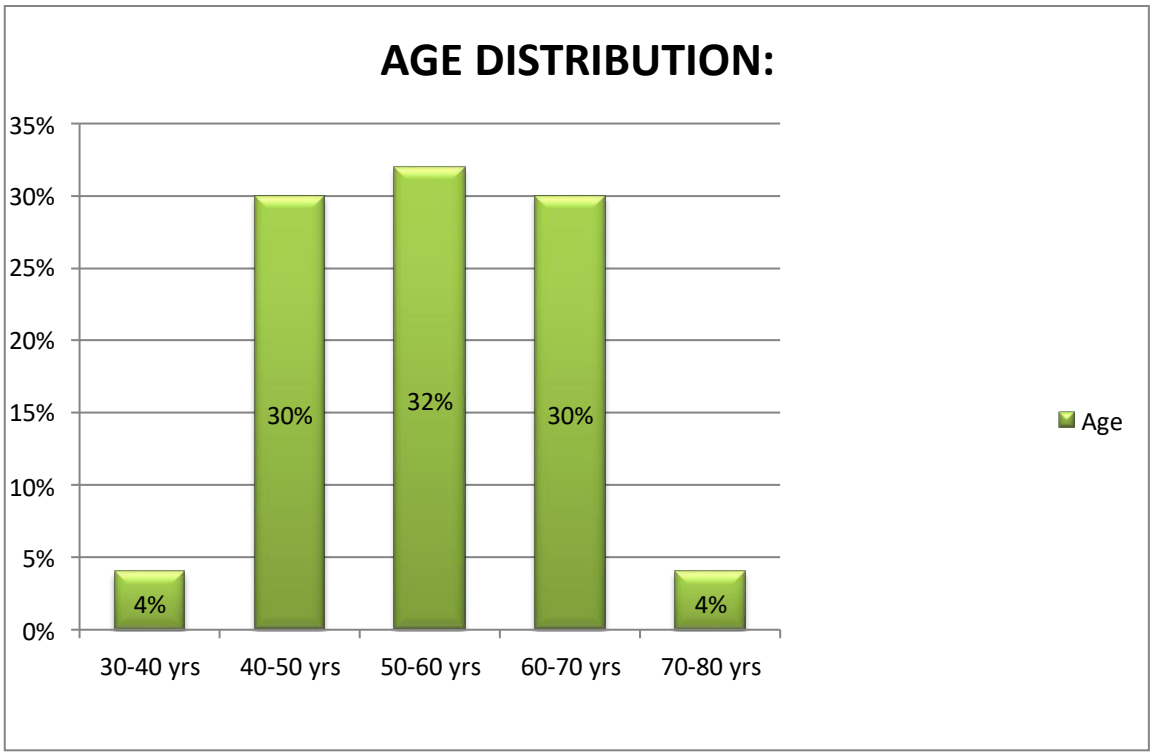


Table 2 : SEX DISTRIBUTION

Among the 50 patiets with Diabetic Maculopathy, 21 were females and 29 were males. There was a male preponderance in the group.

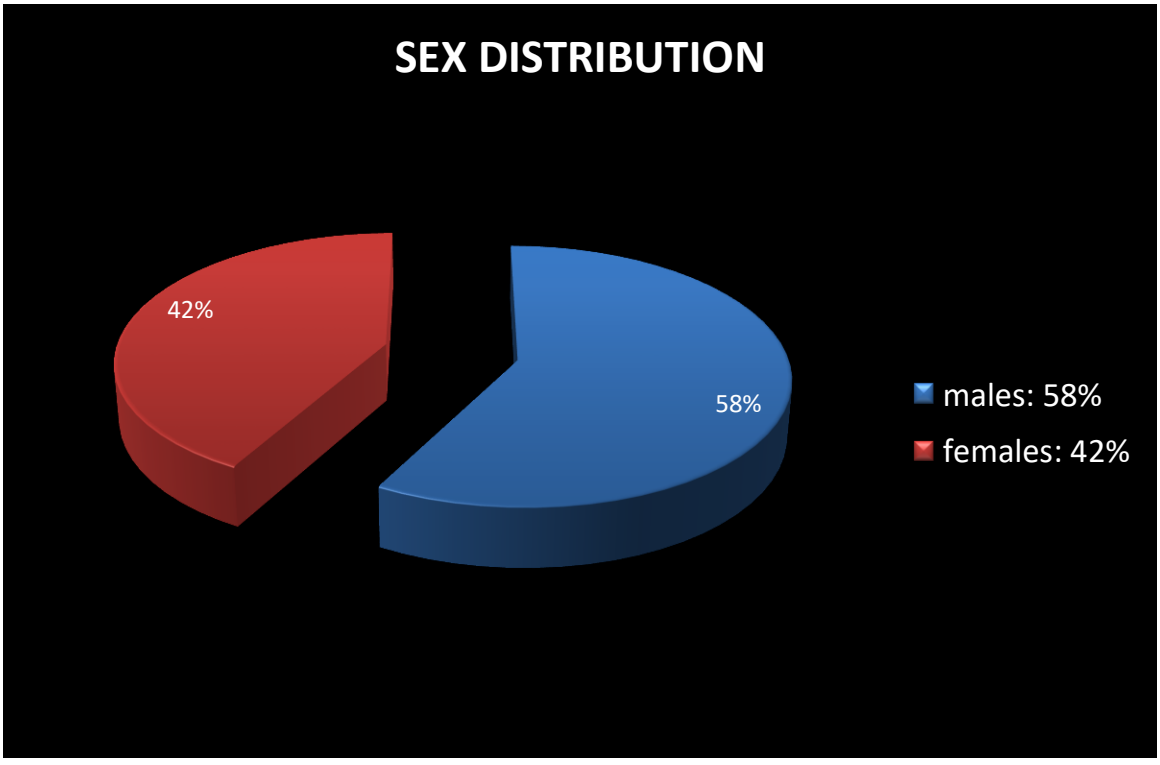


Table 3 : PERCENTAGE DISTRIBUTION IN EYES:

It was found that among the 50 Diabetic patients, 22 patients had Right Eye affected with Maculopathy, 24 patients had Left eye affected with Maculopathy and 4 patients had both eyes affected with Maculopathy. Majority of the patients had Left Eye affected by Diabetic Maculopathy.

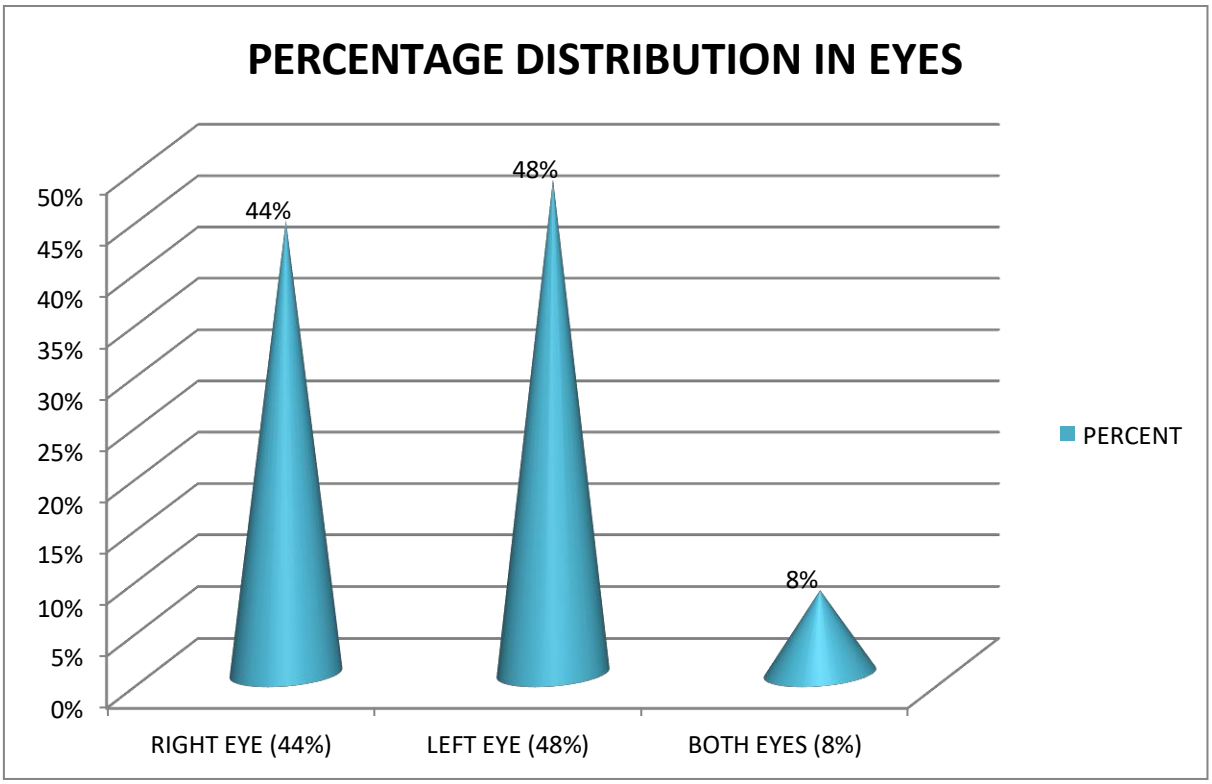


Table 4 :DISTRIBUTION OF OCCUPATION:

Among the 50 patients, occupation plot showed that more were coolies and housewives.

OCCUPATION	NUMBER (out of 50 patients)
COOLIE	16 (32%)
OFFICER	12 (24%)
DRIVER	3 (6%)
HOUSEWIFE	15 (30%)
OTHERS(PAINTER,TAILOR)	4 (8%)

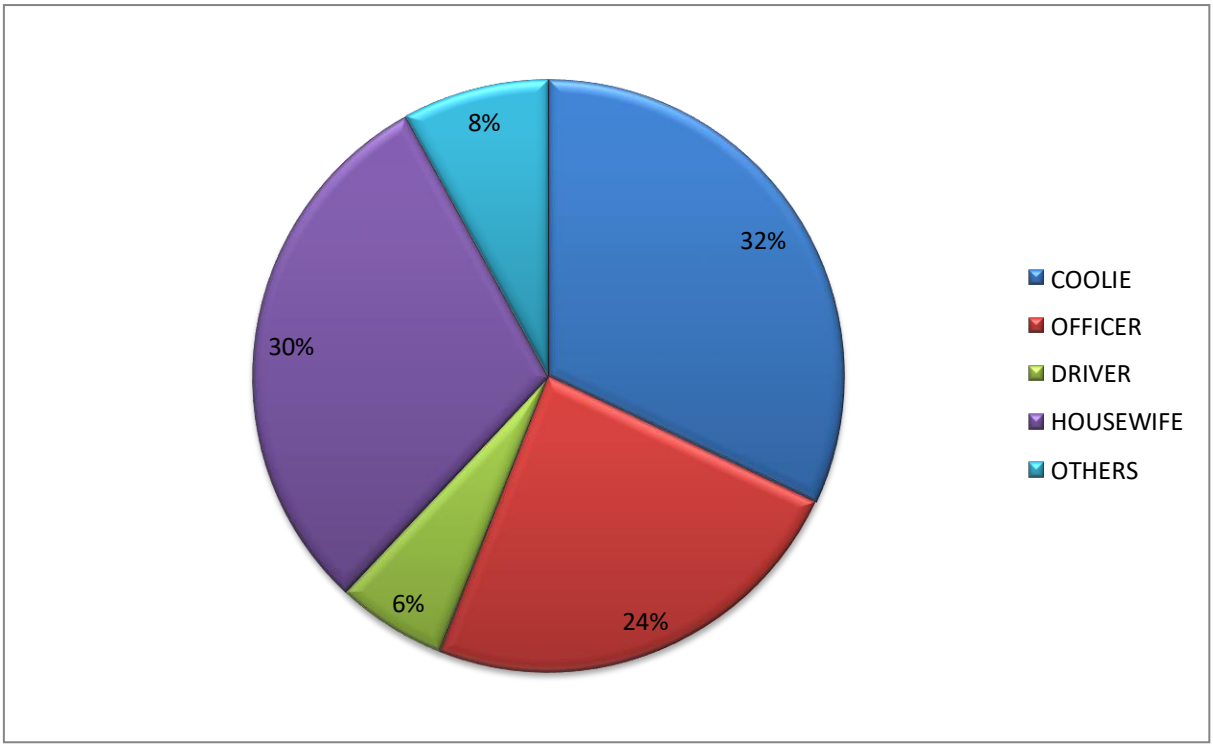


Table 5 :DISTRIBUTION ON BMI:

Acoording to Body Mass Index(BMI) as per South East Asian population standards, the patients in the study were grouped into 3 classes: Normal, overweight and. obese. It was found out that most of the patients had a normal BMI.

BODY MASS INDEX (BMI)	PERCENTAGE
18.5-22.5 (Normal)	25 (50%)
22.5-25 (overweight)	17 (34%)
>25 (obese)	8 (16%)

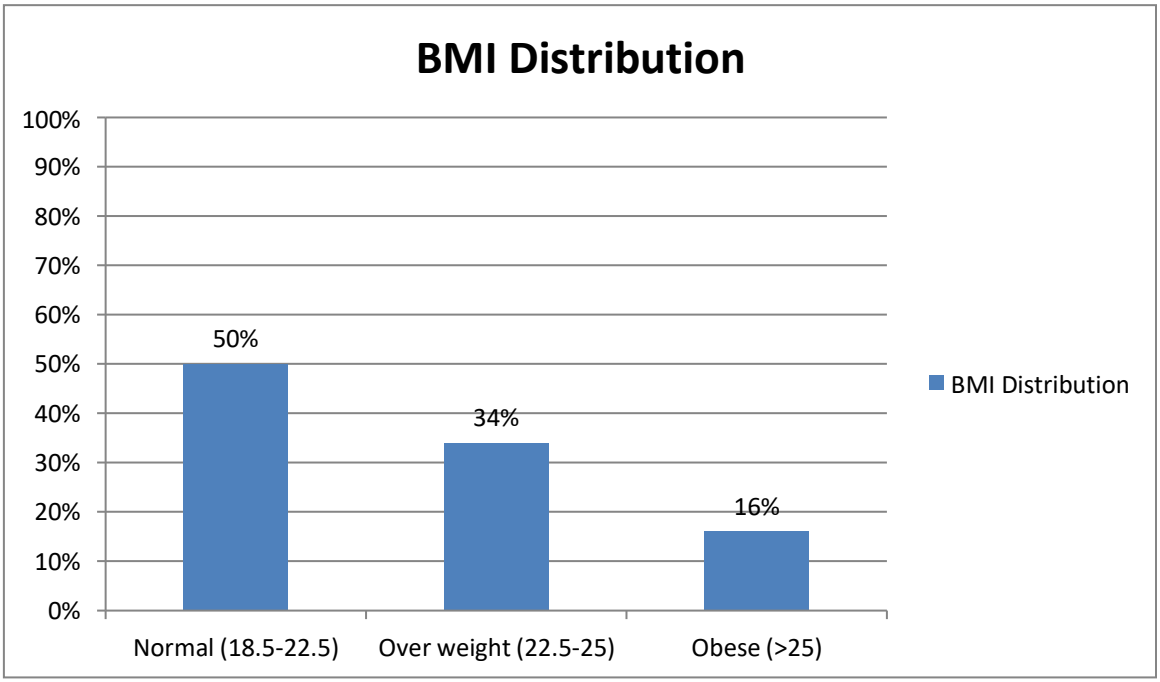


Table 6 : COMPARISON OF LIPID PROFILE:

Among the 50 Diabetic patients, fasting lipid profile showed that 19 had no abnormality,18 had higher cholesterol levels,9 had high Triglycerides and 4 had high LDL in blood.

Lipid Profile	n (%)
Cholesterol	18 (36.0)
LDL	4 (8.0)
Triglycerides	9 (18.0)
Normal	19 (38.0)
Total	50 (100.0)

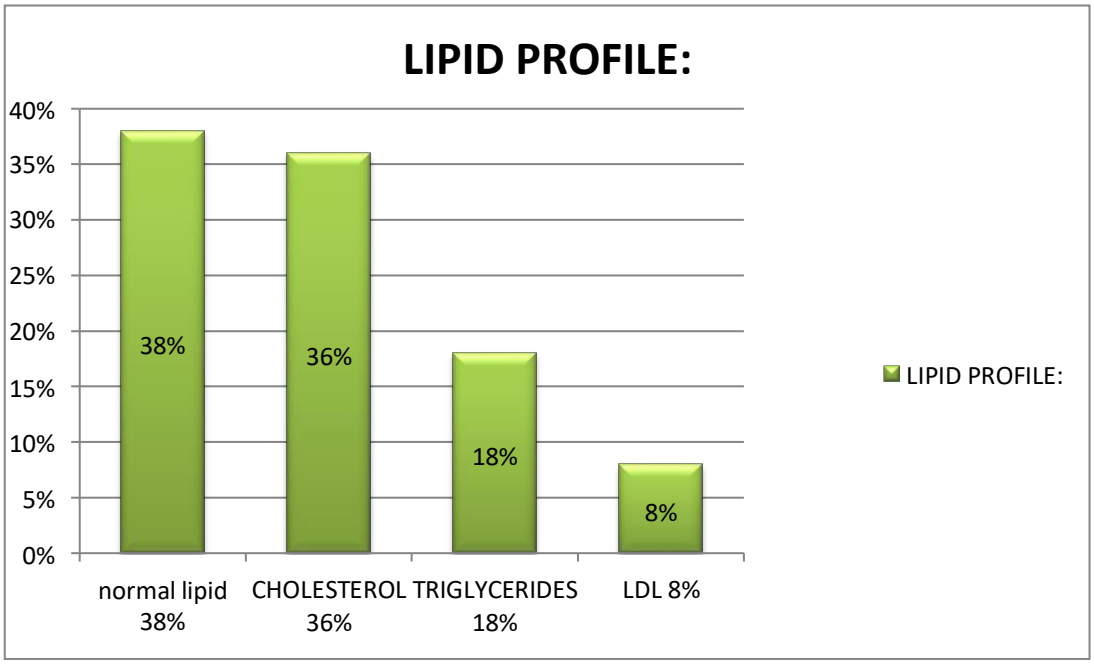


Table 7 :COMPARISON OF TOTAL FFA FINDINGS:

Among the 50 DiabeticMaculopathy patients, the Fundus fluorescein Angiography showed 2 main patterns:

1. **Ischemic maculopathy**(increased FAZ size and capillary nonperfusion areas)

2. **Blocked fluorescence** (CSME due to hard exudates and areas of leakage from microaneurysms)

It was seen that the patients with Blocked fluorescence outnumbered those with Ischemic maculopathy

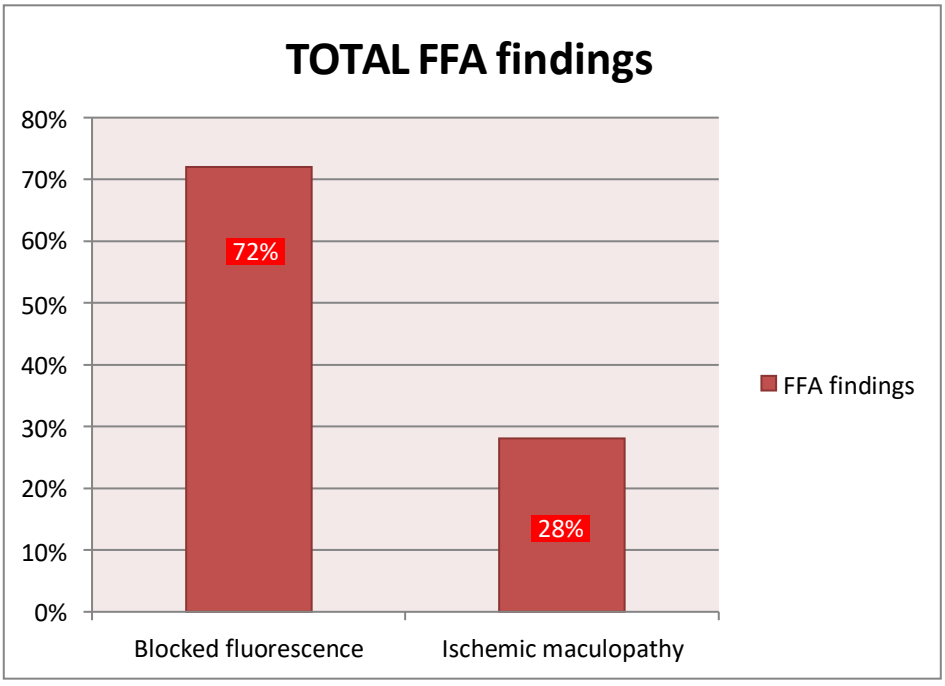


Table 8 :FFA FINDINGS IN PATIENTS WITH HIGH CHOLESTEROL:

Among the 50 patients, 18 had high cholesterol levels in Lipid profile. On FFA, 17 showed Blocked fluorescence and 1 showed Ischemic Maculopathy. Patients with high cholesterol had developed more blocked fluorescence in FFA (p value 0.042) statistically significant

Lipid Profile	FFA	
	Blocked Fluorescence due to HE n (%)	Ischemic Maculopathy(↑FAZ) n (%)
Cholesterol	17 (58.6)	1 (12.5)
Normal	12 (41.4)	7 (87.5)
Total	29 (100.0)	8 (100.0)
p value	0.042– Significant	

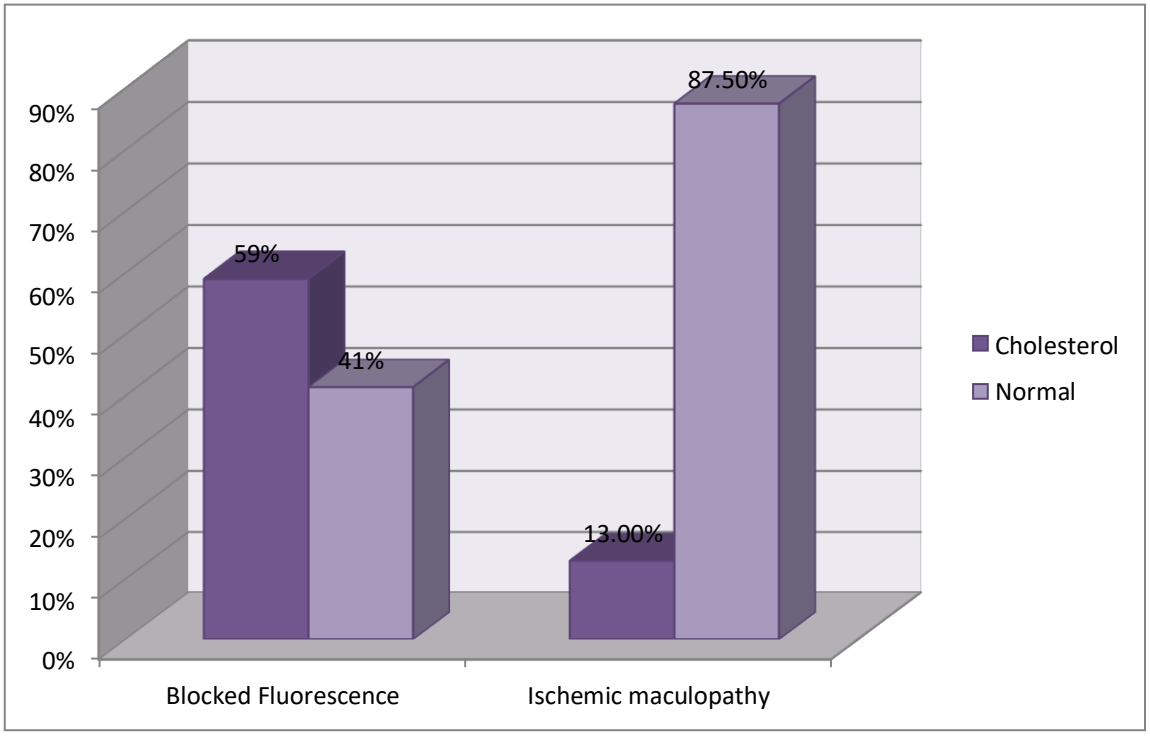


Table 9 :FFA FINDINGS IN PATIENTS WITH HIGH TRIGLYCERIDES:

Among the 50 patients, 9 had increased levels of Triglycerides in Lipid profile. On FFA, 5 showed Blocked fluorescence and 4 showed Ischemic Maculopathy.

Lipid Profile	FFA	
	Blocked Fluorescence due to HE n (%)	Ischemic Maculopathy(↑FAZ) n (%)
Triglycerides	5 (29.4)	4 (36.4)
Normal	12 (70.6)	7 (63.6)
Total	17 (100.0)	11 (100.0)
p value	1.000– Not Significant	

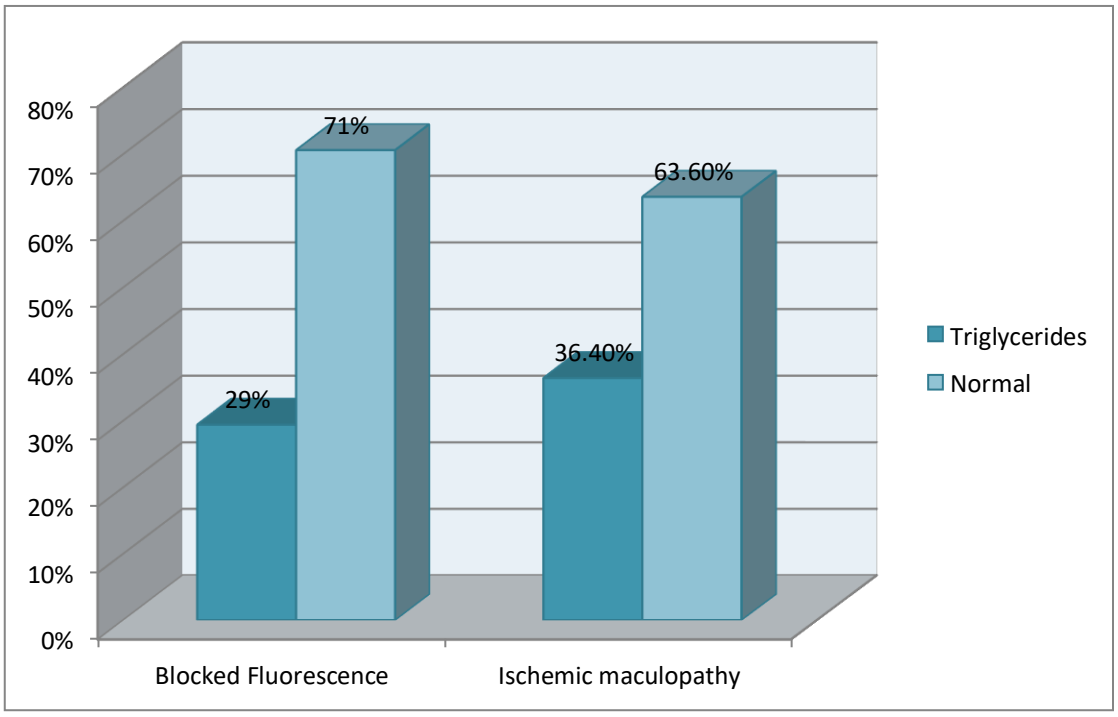


Table 10 :FFA FINDINGS IN PATIENTS WITH HIGH LDL:

Among the 50 patients, 4 had high LDL levels in Lipid profile. On FFA, 2 showed Blocked fluorescence and 2 showed Ischemic Maculopathy.

Lipid Profile	FFA	
	Blocked Fluorescence due to HE n (%)	Ischemic Maculopathy(↑FAZ) n (%)
LDL	2 (14.3)	2 (22.2)
Normal	12 (85.7)	7 (77.8)
Total	14 (100.0)	9 (100.0)
p value	1.000– Not Significant	

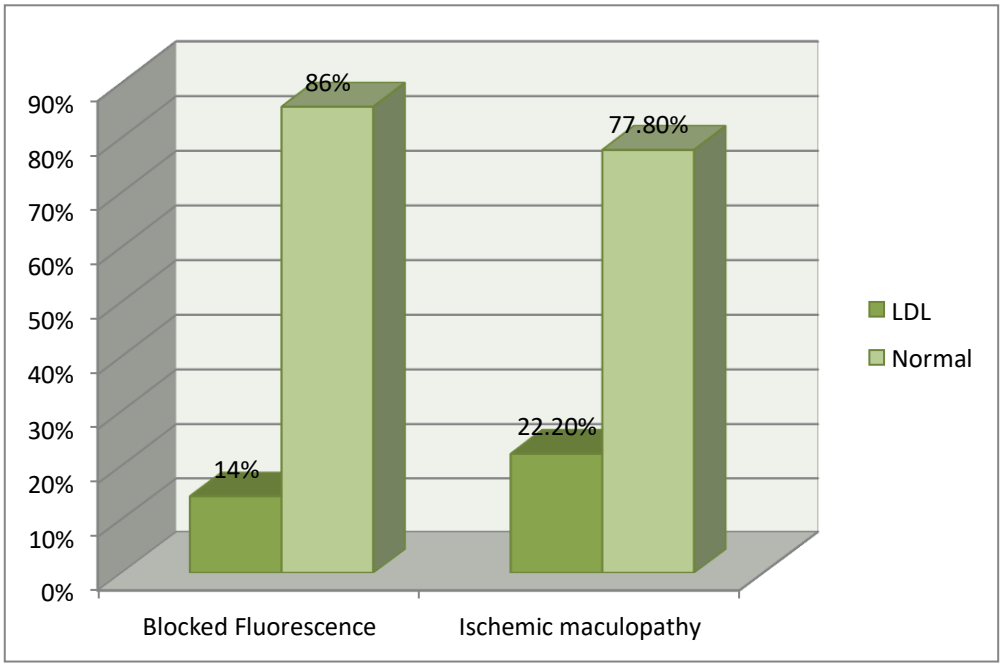
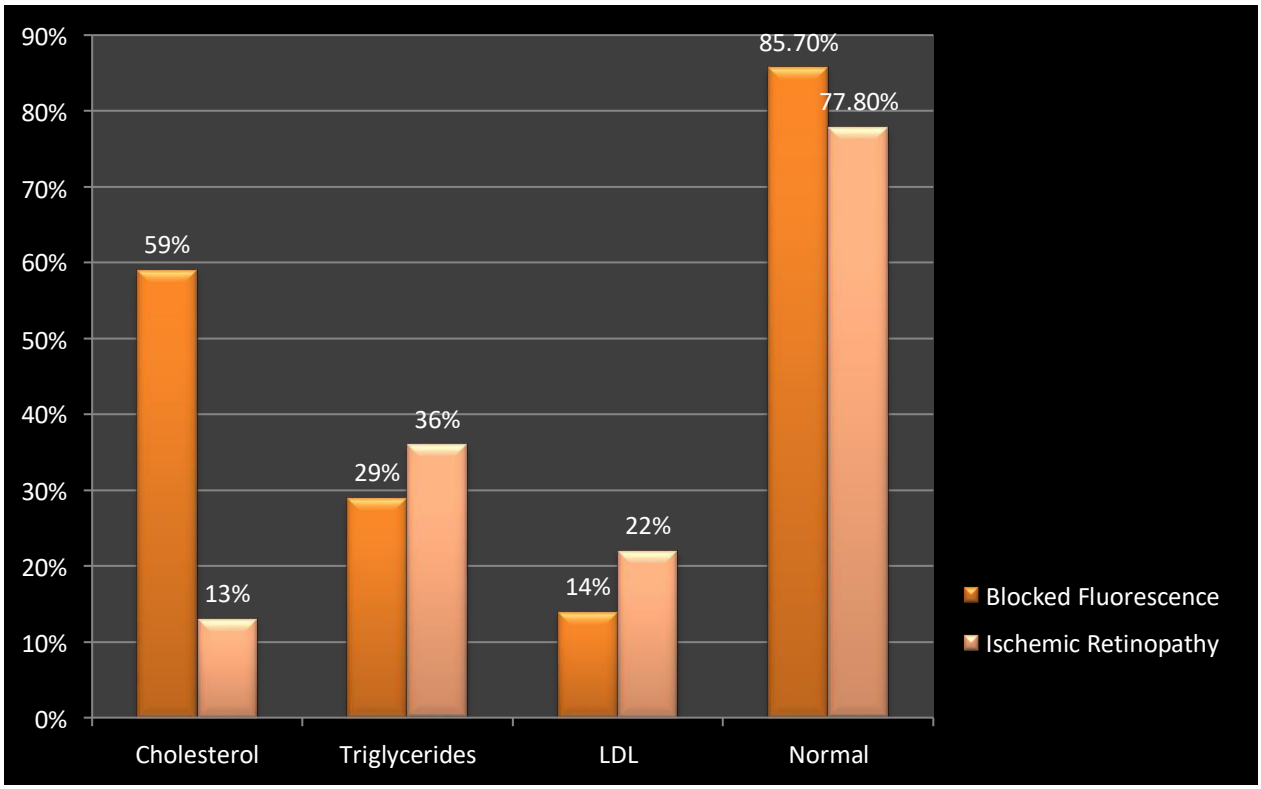


Table 11 :COMPARISON OF FFA FINDINGS :

Among the 50 patients with Diabetic Maculopathy, the FFA findings of Blocked fluorescence was seen more statistically significant among those dyslipidemic patients who had high cholesterol.



SUMMARY:

- Age distribution in the group varied from 30-80 years. They were categorised into 5 classes with a class interval of 10years each. Majority of Diabetics developed Diabetic Maculopathy between the range of 50-60 years of age.

- Among the 50 patiets with Diabetic Maculopathy, 21 were females and 29 were males. There was a male preponderance in the group.

- It was found that among the 50 Diabetic patients, 22 patients had Right Eye affected with Maculopathy, 24 patients had Left eye affected with Maculopathyand 4 patients had both eyes affected with Maculopathy. Majority of the patients had Left Eye affected by Diabetic Maculopathy.

- Among the 50 patients, occupation plot showed that more were coolies and housewives. But high serum cholesterol levels were seen in patients with sedentary work.

- Acoording to Body Mass Index(BMI) as per South East Asian population standards, the patients in the study were grouped into 3 classes: Normal, overweight and. obese. It was found out that most of the patients had a normal BMI.

- Among the 50 Diabetic patients, fasting lipid profile showed that 19 had no abnormality,18 had higher cholesterol levels,9 had high Triglycerides and 4 had high LDL in blood.

- Among the 50 Diabetic Maculopathy patients, the Fundus fluorescein Angiography showed 2 main patterns: Blocked Fluorescence and Ischemic Maculopathy. It was seen that the patients with Blocked fluorescence outnumbered those with Ischemic maculopathy.

- Among the 50 patients, 18 had high cholesterol levels in Lipid profile. On FFA, 17 showed Blocked fluorescence and 1 showed Ischemic Maculopathy.

-Among the 50 patients, 9 had increased levels of Triglycerides in Lipid profile. On FFA, 5 showed Blocked fluorescence and 4 showed Ischemic Maculopathy.

- Among the 50 patients, 4 had high LDL levels in Lipid profile. On FFA, 2 showed Blocked fluorescence and 2 showed Ischemic Maculopathy.

-Hence, aamong the 50 patients with Diabetic Maculopathy, the FFA findings of Blocked fluorescence was seen more statistically significant among those dyslipidemic patients who had high cholesterol wih a p value of 0.042.

-But the relation between high triglycerides and high LDL to the presence of Blocked Fluorescence in FFa was not statistically significant(p value 1.00)

DISCUSSION:

The Indian population is considered to have an unusually efficient glucose metabolism. With the advent of modernisation and westernisation among Indians, the eventual weight gain and sedentary lifestyle, the former advantage is lost and incidence of diabetes has increased. Now the disease is claiming its toll. With the high prevalence of diabetes, concerns on its morbid complications like Diabetic Retinopathy are also increasing.

Hyperglycemia and Dyslipidemia account for the two major metabolic disorders seen in patients with diabetes mellitus. The role of diabetic dyslipidemia in the development of microvascular complications has not gained much attention or depth in world wide literature.

The present study had a near equal sex distribution with only a slight male predominance. Similar male preponderance was also seen in the CURES Eye study, UKPDS studyGupta et al and the Andhra Pradesh Eye Disease study (APEDS).

The relationship of retinopathy with age was in concordance to that found in many other studies which marked an increased prevalence of Diabetic Retinopathy with increasing age. Dondana et al CURES Eye Study and APED Study also have found significant correlation between the patient age and diabetic retinopathy.

Epidemiological Study of Diabetic Retinopathy (WESDR) also found that risk of retinopathy is directly related to the duration of diabetes. In India, virtually all studies have shown an increased prevalence of DR as the duration of diabetes increased (Gupta et al, APEDS study, Agarwal et al).

The CURES Eye Study observed a linear trend between prevalence of DR and poor glycemic control. Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) found that risk of retinopathy is related to the control of blood glucose levels.

The present study showed statistically significant correlation between diabetic maculopathy (with edema, hard exudates and blocked fluorescence) with raised total cholesterol level ($p = 0.042$). Increased cholesterol level was significantly associated with the occurrence of all grades of retinopathy among Diabetics. However

Correlation between Triglycerides and LDL was not statistically significant ($p = 1.0$). Al-Bdour et al and Larsson et al also found significant correlation between higher levels of serum total cholesterol and retinopathy. Rema et al (CURES eye study) and Haddad et al found that both serum triglyceride ($p= 0.001$) levels and total cholesterol ($P= 0.014$) were higher in patients with diabetic retinopathy as compared to those without diabetic retinopathy. In contrast to the present study, Gupta et al demonstrated that diabetics with raised LDL levels showed higher prevalence of Diabetic

retinopathy (38%) compared to others (28.3%) (p=0.05). Lyons et al and the EURODIAB Complications Study found that triglyceride level was related to all levels of retinopathy.

The significant association between hypercholesterolemia and CSME goes in accordance with the study by Al-Bdour et al Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR) and CURES eye study.

The drawbacks of the study are that Optical Coherence Tomography(OCT) was not done for all the patients. In such conditions it is more common to underestimate than to overestimate fundus changes related to diabetic retinopathy. In the present study CSME was diagnosed by Slit lamp biomicroscopy with 78D/ 90D lens and Ischemic Maculopathy diagnosed by Fundus Fluorescein Angiography. Because of the non-availability, the newer, the more sensitive method of assessing retinal thickening such as with optical coherence tomography were not used. The study did not evaluate other risk factors for the development of retinopathy like anemia. Also, the referral of uncontrolled diabetics who could not be included in the study, would have allowed the possibility of selection bias to creep into the study.

CONCLUSION:

The present study demonstrated statistically significant correlation between diabetic retinopathy and hypercholesterolemia (p value 0.042). Increased cholesterol level was significantly associated with the occurrence of all grades of retinopathy. It also showed that hypercholesterolemia is significantly associated with CSME. It has been observed that the appearance of hard exudates is consistent with the appearance of dyslipidaemia, which is typical for diabetic patients. The aim of this paper was to underline the role of elevated serum lipids in the onset of diabetic macular oedema and hard exudates. The analysis of the severity of hard exudates and edema in relation to lipid fractions in the examined group showed that total cholesterol was significantly higher in such patients. Hyperlipidaemia is a risk factor for the development of hard exudatesin patients with diabetic maculopathy. The current treatment for diabetic retinopathy is laser photocoagulation. With the advent of systemic lipid lowering therapy over the last two decades, there may be potential for medical therapy also to control dyslipidemic in diabetics thus reducing their progression to macular edema. There is some anecdotal evidence of the effect of lipid lowering agents in reducing hard exudates. Further studies are required to establish the causal relationship between dyslipidemia and diabetic retinopathy. If established, these data can lend additional support to current treatment guidelines recommending aggressive lowering of elevated

lipids among diabetic patients. Efficient lipid control, in addition to its known health benefits in preventing cardiovascular disease, can also lessen the ocular morbidity and associated health care costs, thereby potentially improving the quality of life and vision among people with type 2 diabetes who are more prone to develop Diabetic Macular Edema.

ANNEXURES

BIBLIOGRAPHY

1. Diabetic maculopathy and Fundus fluorescein Angiography.EyeWiki. Wikipedia ,The free encyclopedia

2. Rosenblatt B, Benson W (2003); Kanski"s Clinical Ophthalmology: A systematic approach. Kanski JU, editor. London: Butterworth and Heinemann.

3. Kanski JJ. Retinal vascular diseases. Chapter 16, In : Clinical ophthalmology – A systemic approach, 6th edn. New Delhi: Elsevier; 2007

4. Rema M, Srivastava BK, Anitha B, Deepa R, Mohan V. Association of serum lipids with diabetic retinopathy in urban South Indians-the Chennai Urban Rural Epidemiology Study (CURES) Eye Study-2. Diabetic Medicine 2006; 23: 1029-1036.

5. SureshaAneplaRajappa, DeepthiMolleti, Nandini C, DonepudiGayatri Devi and KudacheJanhaviAbhay SA Rajappa (2014); Role of fundus fluorescein angiography in macular disorders International Journal of BiomedicalResearch, I JBR, 05 (10)

6. Sharma RA. Diabetic eye disease in southern India. J Comm Eye Health 1996; 09(20): 56-58.

7. Stephen Ryan. RETINA.4th ed. Vol. II.Chapter 66. In: Etiologic mechanisms in Diabetic retinopathy, Robert N. Frank, eds. Philadelphia PA: Elsevier; 2006: 1241 - 1265

8. Albert, Jakobiec. In: Principles and practice of ophthalmology. 3rd Edn., 1743-1800.

9. Hamilton AMP, Ulbig MW, Polkinghorne P. Management of diabetic retinopathy. BMJ Publishing group, London, 1996.

10. Sankaranethralaya (2014); Fundus fluorescein angiography (FFA)

11. Karan A K (2011); Diabetic retinopathy, Jan 30.

12. PriyankGarg, Samarth Agarwal, ArindanChakravarti et al (2011); diabetic maculopathy, e journal of ophthalmology, www.eophtha.com

13. Epidemiologic Study of Diabetic Retinopathy (WESDR), XIII: relationship between serum cholesterol to retinopathy and hard exudate. Ophthalmology 1991; 98: 1261-5.

14. A K Khurana Textbook of Comprehensive Ophthalmology 2007.chapter 11.Diseases of the Retina.Page 260.

15. CME series in Ophthalmology No.3 All India Ophthalmological Society(AIOS) Management of Diabetic Retinopathy

16. Retinal Vascular Disorders.(Dr.K.Chandra Mohan, Dr DhananjayShukla, .Dr.R. Kim) AravindEyaHospital.Chapter 4.Diabetic Retinopathy.

PROFORMA

NAME: IP/OP NO:

AGE:

SEX: FAMILY HISTORY:

INVESTIGATIONS:

OCULAR EXAMINATION:

SLIT LAMP EXAMINATION:

Right eye		Left eye
	Conjunctiva	
	Cornea	
	Anterior chamber	
	Iris	
	Pupil	
	Lens	
	Fundus: Indirect 90 D Media Optic disc C:D rato Vessels A:V ratio Background Macula Grade of Diabetic Retinopathy	

FUNDUS FLOURESCEIN ANGIOGRAPHY FINDINGS:

EARLY PHASE OF FFA:

Right eye		Left eye
Present/absent		Present/absent
	Leakage in perifoveal area	
	Hyperfluorescence areas	

LATE PHASE OF FFA:

Right eye		Left eye
Present/absent		Present/absent
	Leakage in perifoveal area	
	Capillary non perfusion	
	Enlargement of foveal avascular zone	

BIOCHEMICAL TESTS: DATE OF TEST FINDING

FBS		
PPBS		
HBA1C		
LIPID PROFILE		
HDL		
LDL		
TRIGLYCERIDE		
SERUM CREATININE		
Urine: Albumin Sugar Deposits		

MASTER CHART

Sl No	NAME	AGE	SEX	WORK	EYE	BMI	LIPID PROFILE	FFA
1	Shekar	62	M	Officer	LE	23	Cholesterol	Blocked Fluo. due to HE
2	Kalyani	31	F	Housewife	RE	19	Normal	Isch. Maculopathy (↑FAZ)
3	Shanthi	46	F	Housewife	LE	24	Cholesterol	Blocked Fluo. due to HE
4	Thangaraj	41	M	Coolie	RE	26	LDL	Blocked Fluo. due to HE
5	Vijaya	65	F	Officer	LE	24.5	Triglycerides	Blocked Fluo. due to HE
6	Anbuchelvam	51	M	Coolie	RE	27	Cholesterol	Blocked Fluo. due to HE
7	Ganeshan	68	M	Coolie	BE	24	Cholesterol	Blocked Fluo. due to HE
8	Raja	52	M	Coolie	RE	24.5	LDL	Isch. Maculopathy (↑FAZ)
9	Amritham	71	F	Housewife	LE	20	Normal	Blocked Fluo. due to HE
10	Palraj	54	M	Coolie	RE	23	Triglycerides	Isch. Maculopathy (↑FAZ)
11	Veerammal	56	F	Housewife	LE	24	Cholesterol	Blocked Fluo. due to HE
12	Panju	69	F	Coolie	LE	22.5	LDL	Isch. Maculopathy (↑FAZ)
13	Kamala	52	F	Officer	LE	25.5	Cholesterol	Blocked Fluo. due to HE
14	Varatharajan	48	M	Officer	RE	26	Cholesterol	Blocked Fluo. due to HE
15	Bhuvaneshwari	74	F	Housewife	LE	19.5	Normal	Blocked Fluo. due to HE
16	Senthil	46	M	Officer	BE	24	Cholesterol	Isch. Maculopathy (↑FAZ)
17	Kannayya	61	M	Coolie	RE	21.5	Normal	Isch. Maculopathy (↑FAZ)
18	Shanmugam	52	M	Driver	RE	24	Triglycerides	Isch. Maculopathy (↑FAZ)
19	Ganga Devi	57	F	Housewife	RE	23.5	Triglycerides	Blocked Fluo. due to HE
20	Pandiyammal	61	F	Coolie	LE	20	Normal	Blocked Fluo. due to HE
21	Alagammal	48	F	Housewife	RE	25	Cholesterol	Blocked Fluo. due to HE
22	Ramjaan Beevi	66	F	Housewife	LE	19.5	Normal	Isch. Maculopathy (↑FAZ)
23	Krishnan	41	M	Officer	LE	21	Triglycerides	Blocked Fluo. due to HE
24	Mathiyalagan	42	M	Coolie	RE	23	Cholesterol	Blocked Fluo. due to HE
25	Poongothai	47	F	Officer	LE	18.5	Normal	Blocked Fluo. due to HE

Sl No	NAME	AGE	SEX	WORK	EYE	BMI	LIPID PROFILE	FFA
26	Anna Lakshmi	49	F	Housewife	BE	24	Cholesterol	Blocked Fluo. due to HE
27	Muthu Krishnan	39	M	Tailor	RE	22	Normal	Blocked Fluo. due to HE
28	Gunashegaran	55	M	Driver	LE	19.5	Triglycerides	Isch. Maculopathy (↑FAZ)
29	Subramani	53	M	Driver	LE	21	LDL	Blocked Fluo. due to HE
30	Aadhi	61	F	Housewife	RE	21	Normal	Isch. Maculopathy (↑FAZ)
31	Ganga	62	F	Housewife	RE	25	Cholesterol	Blocked Fluo. due to HE
32	Jayaraj	54	M	Officer	LE	23	Triglycerides	Blocked Fluo. due to HE
33	Muthu	57	M	Painter	LE	19.5	Normal	Blocked Fluo. due to HE
34	Dakshinamurthy	48	M	Officer	RE	18.5	Normal	Blocked Fluo. due to HE
35	Kalyana Sundaram	45	M	Officer	LE	24	Normal	Blocked Fluo. due to HE
36	Mallika	67	F	Housewife	RE	19.5	Triglycerides	Isch. Maculopathy (↑FAZ)
37	Chinnaiyya	46	M	Coolie	LE	21.0	Normal	Blocked Fluo. due to HE
38	Ram Jagan	45	M	Coolie	BE	25.5	Cholesterol	Blocked Fluo. due to HE
39	Koothan	68	M	Coolie	RE	19.5	Normal	Isch. Maculopathy (↑FAZ)
40	Ponnusamy	57	M	Officer	LE	26	Cholesterol	Blocked Fluo. due to HE
41	Saravanan	67	M	Coolie	RE	21	Normal	Blocked Fluo. due to HE
42	Chellaiyya	56	M	Coolie	RE	24	Cholesterol	Blocked Fluo. due to HE
43	Kalyani	48	F	Tailor	LE	20	Normal	Blocked Fluo. due to HE
44	Veeranan	58	M	Carpenter	RE	21	Cholesterol	Blocked Fluo. due to HE
45	Moideen Beevi	61	F	Housewife	LE	19.5	Normal	Isch. Maculopathy (↑FAZ)
46	Mani	49	M	Coolie	LE	18.5	Normal	Blocked Fluo. due to HE
47	Velu	52	M	Officer	RE	24	Cholesterol	Blocked Fluo. due to HE
48	Mariyammal	62	F	Housewife	LE	25	Cholesterol	Blocked Fluo. due to HE
49	Pitchai	51	M	Coolie	RE	21	Normal	Isch. Maculopathy (↑FAZ)
50	Gomathi	64	F	Housewife	LE	21.5	Triglycerides	Blocked Fluo. due to HE

LIST OF ABBREVIATIONS:

DR- Diabetic Retinopathy

NPDR- Non Proliferative Diabetic Retinopathy

PDR- Proliferative Diabetic Retinopathy

DME- Diabetic Macular Edema

CSME- Clinically Significant Macular Edema

FAZ- Foveal Avascular Zone

FFA- Fundus Fluorescein Angiography

OCT- Optical Coherence Tomography

CNP- Capillary Non-Perfusion

IRMA- Intra Retinal Microvascular Abnormalities

RE- Right Eye

LE- Left Eye

BMI- Body Mass Index

AGE- Advanced GlycationEndproducts

LDL- Low Density Lipoproteins

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University,
Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.Sruthi. R.S.
Course	:	PG in MS., Ophthalmology
Period of Study	:	2015-2018
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	An Analytical study to evaluate the Association between fundus fluorescein Angiographic changes in diabetic maculopathy and dyslipidemia
Ethical Committee as on	:	21.04.2017

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary Chairman Dean / Convenor

Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
CHAIRMAN
IEC - Madurai Medical College
Madurai

Madurai Medical Colle
Madurai-20

Dissertation on "AN ANALYTICAL STUDY TO EVALUATE THE ASSOCIATION BETWEEN FUNDUS FLUORESCEIN ANGIOGRAPHIC CHANGES IN DIABETIC MACULOPATHY AND DYSLIPIDAEMIA"

Submitted in partial fulfillment of requirements of MASTER OF SURGERY DEGREE

BRANCH – III – (OPHTHALMOLOGY)

GOVT. RAJAJI HOSPITAL, MADURAI MEDICAL COLLEGE

MADURAI- 20

THE TAMILNADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI

2018

INTRODUCTION: The incidence of Type 2 Diabetes Mellitus is turning out to be a near epidemic in India, and so is its complications like Diabetic retinopathy. Many of these patients belong to productive socioeconomic age group. Therefore identifying the risk factors for Diabetic Macular Edema and keeping them under check is of paramount importance in saving the vision of Diabetics, reducing morbidity and thus reducing the economic burden due to blindness in our country. Diabetic retinopathy (DR) is a leading cause of visual disability and blindness among Diabetics. It is a major microvascular complication of diabetes and is frequently

CERTIFICATE

This is to certify that this dissertation entitled **"AN ANALYTICAL STUDY TO EVALUATE THE ASSOCIATION BETWEEN FUNDUS FLUORESCEIN ANGIOGRAPHIC CHANGES IN DIABETIC MACULOPATHY AND DYSLIPIDAEMIA"** of the candidate **Dr.SRUTHI.R.S,** with Registration number **221513104** for the award of M.S. Degree in the Branch of Ophthalmology (III). I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from Introduction to Conclusion page and Result shows **0 percentage** of plagiarism in the dissertation.

Guide & Supervisor (Sign with Seal)