A DISSERTATION ON

A STUDY TO EVALUATE THE ASSOCIATED SYSTEMIC RISK FACTORS IN TYPE 2 DIABETES MELLITUS PATIENTS WITH CLINICALLY SIGNIFICANT MACULAR EDEMA

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THE TAMIL NADU DR. MGR. MEDICAL UNIVERSITY,

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M.S. DEGREE -BRANCH-III

OPHTHALMOLOGY

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SALEM, TAMILNADU.

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A STUDY TO EVALUATE THE ASSOCIATED SYSTEMIC RISK FACTORS IN TYPE 2 DIABETES MELLITUS PATIENTS WITH CLINICALLY SIGNIFICANT MACULAR OEDEMA

PART I

1. INTRODUCTION Clinically significant macular oedema is one of the major causes of preventable blindness across the world in both developing countries like INDIA and developed countries. Clinically significant macular oedema is one of the major causes of legal blindness mainly in working age group population. As the prevalence of diabetes has already reached epidemic proportions due to increase in aging population and sedentary lifestyle, the early identification of the risk factors for diabetic macular oedema and early prevention of the same becomes essential to prevent vision loss. According to data from International Diabetes Federation Atlas – Eight edition Diabetes mellitus affects 425 million people worldwide. In Southeast Asia region in which India is one among the six countries, 82 million people are affected by Type 2 diabetes mellitus and this number is projected to ascent to 151 million by 2045. Total adult population in India is 82,94,91,000 and total cases of diabetes in adults 7,29,46,400 so the prevalence of diabetes in adults is 8.8%. The prevalence of diabetes is increasing in every country, and more than 80% live in low and middle income countries. Prevalence of diabetes in tamilnadu is 10.4% as stated by Indian Council of Medical Research – India Diabetes (ICMR-INDIAB) The prevalence of clinically significant macular oedema is 20% in type 1 DM, in individuals with Type 2 DM on insulin treatment it is 25% and 14% in patients with type 2 DM on oral anti-hyperglycaemic drug as evidenced by Wisconsin Epidemiologic study

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Communication of Decision of the Institutional Ethics Committee(IEC)

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CONTENTS

A STUDY TO EVALUATE THE ASSOCIATED SYSTEMIC RISK FACTORS IN TYPE 2 DIABETES MELLITUS PATIENTS WITH CLINICALLY SIGNIFICANT MACULAR EDEMA

PART I

ABSTRACT

AIM OF THE STUDY: To evaluate the association of systemic risk factors with clinically significant macular edema in type 2 diabetes mellitus patients. **STUDY DESIGN:** A hospital based cross sectional study conducted between October 2017 and September 2019. **METHODOLOGY:** All patients included in the study were subjected to complete ophthalmologic examination by assessing the visual acuity with Snellen chart, slit lamp examination, Fundus examination with direct ophthalmoscope, indirect ophthalmoscope, and slit lamp bio microscopy with +90D lens. Clinically Significant Macular Edema and Diabetic Retinopathy were graded as per Early Treatment Diabetic Retinopathy Study criteria. The detailed history of age of the patient, duration of diabetes mellitus, treatment history were recorded. The body mass index (BMI), abdominal circumference (AC), blood pressure(BP), total cholesterol, low density lipoprotein(LDL), high density lipoprotein(HDL), triglycerides(TG), Hemoglobin(Hb), Fasting Blood Glucose(FBG), Post prandial Blood Sugar (PPBS), HbA1c, serumcreatinine and proteinuria were collected. To find the significance in categorical data Chi-square test and fischer exact test were used. P value of <0.05 is considered as statistically significant. **RESULTS**: On analysis of multiple risk factors focal maculopathy had significant association with body mass index with P value

being 0.044.Diffuse maculopathy had significant association with HbA1c with p-value being 0.026. **CONCLUSION**: In the analysis of systemic risk factors, a significant correlation was found to exists between abnormal BMI and focal maculopathy and diffuse maculopathy was associated with increased levels of HbA1c. Patients with more number of risk factors developed Clinically Significant Macular Edema within a period of 5 years, even with adequate glycaemic control.

Key words : clinically significant macular edema, systemic risk factors, diabetes mellitus.

1. INTRODUCTION

Clinically significant macular edema is one of the major causes of preventable blindness across the world in both developing countries like INDIA and developed countries.

Clinically significant macular edema is one of the major causes of legal blindness mainly in working age group population. As the prevalence of diabetes has already reached epidemic proportions due to increase in aging population and sedentary lifestyle, the early identification of the risk factors for diabetic macular oedema and early prevention of the same becomes essential to prevent vision loss.

According to data from International Diabetes Federation Atlas – Eight edition Diabetes mellitus affects 425 million people worldwide. In Southeast Asia region in which India is one among the six countries, 82 million people are affected by Type 2 diabetes mellitus and this number is projected to ascent to 151 million by 2045. Total adult population in India is 82,94,91,000 and total cases of diabetes in adults 7,29,46,400 so the prevalence of diabetes in adults is 8.8%.

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Clinically significant macular oedema and proliferative diabetic retinopathy are the vision threatening complications affecting approximately $1/10^{th}$ of the patients with diabetes mellitus and approximately 50% with clinically significant macular oedema will lose two or more lines of visual acuity in 2 years. So the relative risk of blindness in diabetes patients is approximately 5 times more than in those without diabetes, even after adjusting confounding factors like age, sex, race, socioeconomic status, educational status, systemic blood pressure, smoking habits and body mass index.

Apart from non-modifiable risk factors like age, sex, ethnicity, genetics, the modifiable risk factors plays major role in occurrence and progression of both diabetic retinopathy and clinically significant macular edema. In this study the association of the following modifiable risk factors like body mass index, blood pressure, total cholesterol, low density lipoprotein, high density lipoproteins, triglycerides, fasting blood glucose level, glycosylated haemoglobin, total blood count, serum creatinine, and proteinuria are to be assessed.

The clinical trials like Diabetic Retinopathy Study and Early Treatment Diabetic Retinopathy Study showed that the effective treatment for retinopathy could reduce vision loss by 90%. But the need for regular eye examinations that can aid in timely detection and treatment of diabetic retinopathy is less emphasized.

The identification of risk factors and its control is as important as timely detection of diabetic retinopathy. Assessing the association of systemic risk factors and modifying the same would help in reducing vision loss.

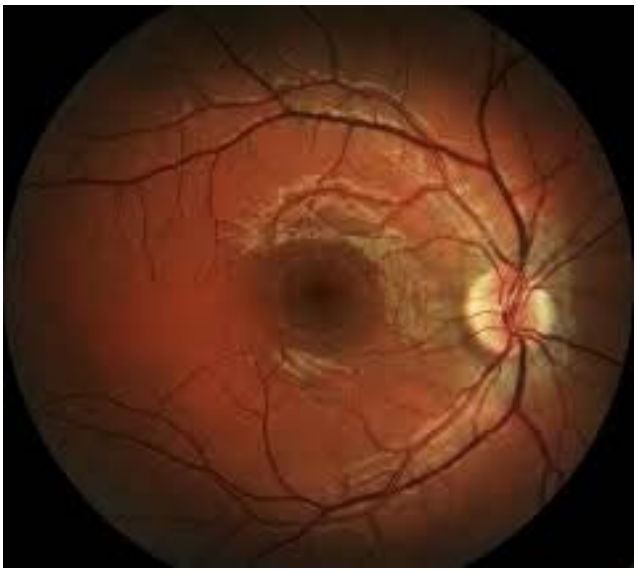
2. ANATOMY OF RETINA AND MACULA

The retina in latin means “network” is made of five fundamental cell types namely neurons, glial cells, blood vessels, microglia and pigment epithelial cells. Developmentally retina is divided into two layers, the pigment layer and the neural layer which are derived from the outer and inner layer of the optic cup respectively. The outer pigment layer gives rise to single layer of retinal pigment epithelium; the inner nuclear layer develops into neuro sensory retina.

The retina is a thin and transparent layer forming the posterior two-thirds of the innermost coat of the eyeball. It extends from the optic disc to the ora serrata and has surface area of 266 sq.mm.

During ophthalmoscopic examination the landmarks of the retina that are visible includes optic disc, the retinal blood vessels, the fovea and the foveola together called as area centralis , the peripheral retina and the ora serrata.

FIGURE 1 : TOPOGRAPHY OF NORMAL RETINA



The area centralis constitutes the fovea and the foveola , the fovea measures 1.85mm and is located at the posterior pole of the globe, 4mm temporal to the centre of the optic disc and 0.8mm below the horizontal meridian, which represents central 5 degrees of visual field.

The foveola measures 0.35mm diameter corresponds only to 1 degree of the visual field and only 0.13mm in thickness because of the presence of cone receptors alone. The foveola appears deeper red than the adjacent retina due to the underlying rich choroidal circulation which shines through the relatively avacular fovea.

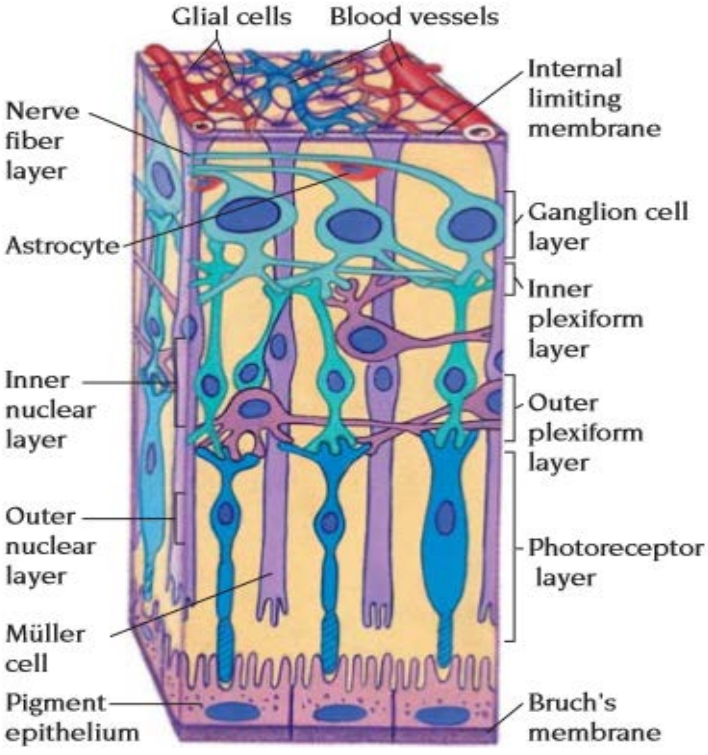
The macula lutea is horizontally oval zone that includes fovea in its centre is 5.5mm in diameter located in between the optic disc and the vascular arcades and it possess faint yellow colouration due to the accumulation of xanthophyll pigment and oxygenated carotenoids like lutein and zeaxanthin in the ganglion and bipolar cells. The area around the fovea of 0.5mm in width is called as parafovea and 1.5mm in width is called as perifovea.

The cross section of the retina is represented by 10 layers from outer to inner as follows

1. Retinal pigment epithelium ,single layer
2. Photoreceptor layer of cones and rods
3. External limiting membrane, fenestrated membrane. Created by zonular attachments between photoreceptors and the outer extent of muller cells
4. Outer nuclear layer, nuclei of rods and cones

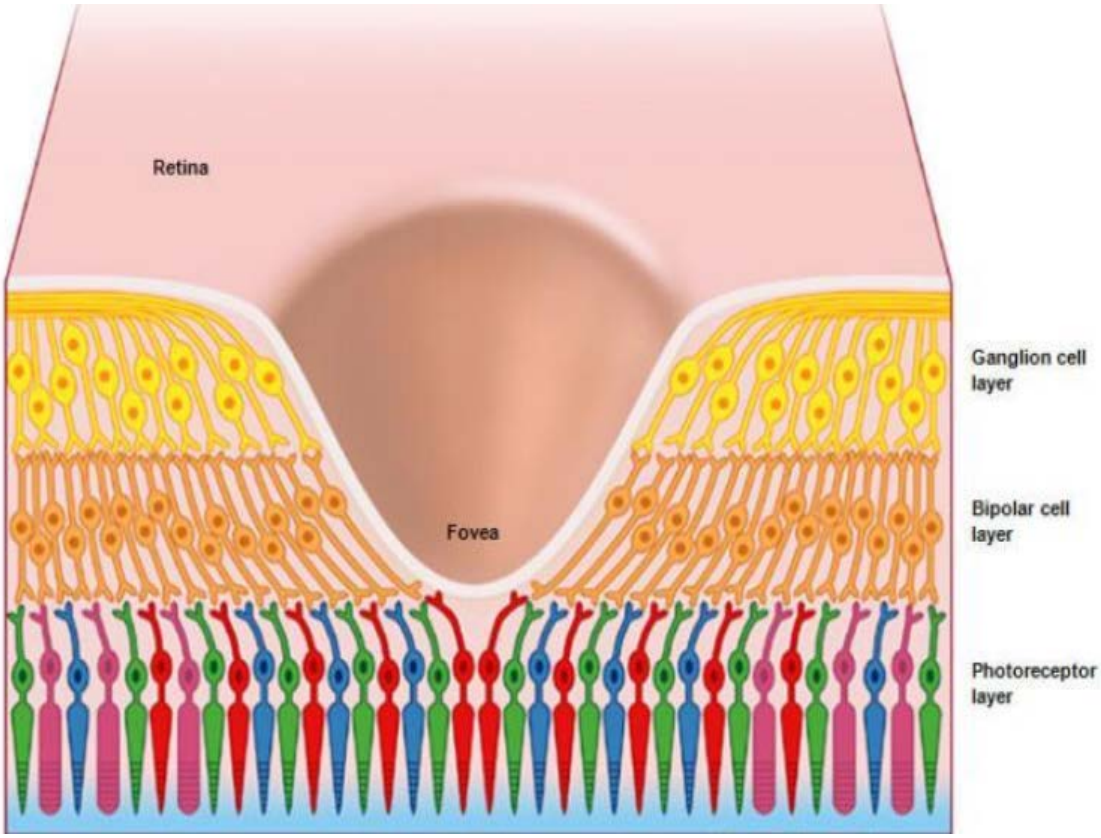
5. Outer plexiform layer, synapses between photoreceptor with bipolar cells. Each cone synapse with midget type of polar cell. More than one rod cell , sometimes even more than 100 rod cells converge on to single bipolar cell.
6. Inner nuclear layer (cell bodies of amacrine cells, horizontal cells, bipolar cells and muller cells.
7. Inner plexiform layer
8. Ganglion cell layer, cell bodies of ganglion cells.
9. Nerve fibre layer formed by the axons of ganglion cells
10. Internal limiting membrane , formed by the foot plates of muller cells, it is made of collagen fibres, laminin, fibronectin acts as an interface between retina and vitreous.

FIGURE 2 : MICROANATOMY OF RETINA



At the fovea only six layers are present which includes from RPE to outer plexiform layer and internal limiting membrane. The inner layers were absent, so that the incident light directly falls on the photoreceptors, thereby scattering of light is reduced. Retinal pigment epitheliums are taller and denser in foveal area than in the periphery. Also there is increased density of pigment in the retinal pigment epithelium.

FIGURE 3 : LAYERS OF FOVEA



Blood supply to retina

Blood supply is by central retinal artery a branch from ophthalmic artery which supplies inner six layers and short posterior ciliary artery which supplies outer four layers. Fovea is relatively an avascular zone. Foveal Avascular Zone (FAZ) measures about 500µm. occasionally a part of the inner retina in macular area is supplied by cilioretinal artery. Venous blood drain through vortex veins into the central retinal vein and leaves the eye. Then via superior ophthalmic and inferior ophthalmic into the cavernous sinus.

Blood retinal barrier

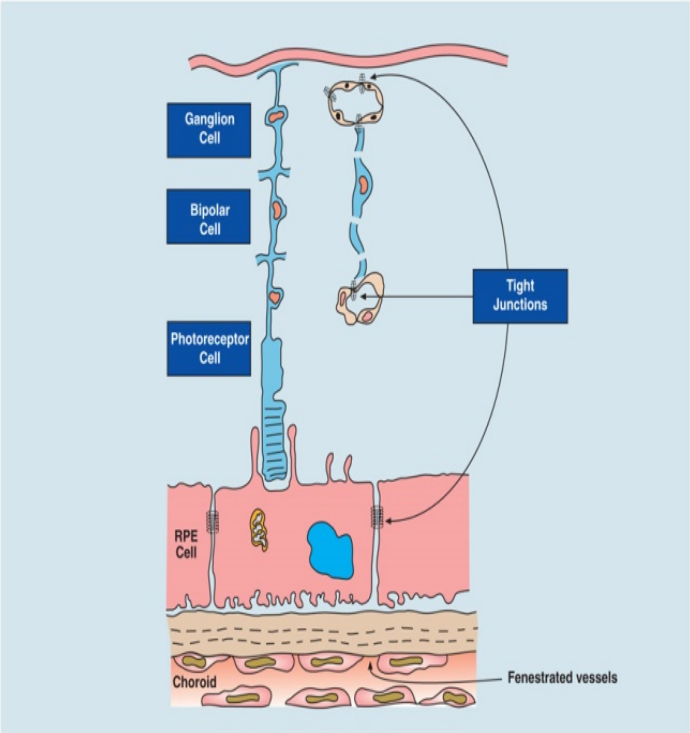
Tight physiological barrier that regulates the movement of ions, proteins and water in and out of the retina.There are two barriers one at the level of RPE by zonula occludentes and another formed by tight junctions between non-fenestrated endothelial cells of retinal capillaries. The outer barrier regulates the flow between choriocapillaries and retina and the inner barrier regulates the transport through retinal capillaries.

The tight junctions perform two main functions

1. Gate function – that restricts the passage of molecules through the paracellular space
2. Fence function- it is the polarity that prevents the movement of lipids and proteins across the apical and basolateral plasma membrane.

There are more than 40 transmembrane proteins present in the tight junctions at the molecular level. The important family of proteins are transmembrane proteins, junctional adhesion molecules, cytoplasmic-scaffold proteins like zonula occludens.

FIGURE 4: OUTER AND INNER BLOOD RETINAL BARRIER SCHEMATIC REPRESENTATION



Schematic representation of blood retinal barrier, inner blood retinal barrier formed by tight junctions between the endothelial cells of retinal capillaries and the outer blood retinal barrier forms by zonula occludens of retinal pigment epithelial cells.

3. DIABETIC MACULAR OEDEMA

DME is one of the main causes of vision loss in diabetic patients. It develops due to the breakdown of blood retinal barrier by changes in tight junction proteins namely occludin and Zonula Occludentes-1, leading to increased vascular permeability and leakage of fluid and exudates. Diabetic maculopathy is characterised by accumulation of extracellular fluid in Henle's layer (outer plexiform layer) and inner nuclear layer of retina. There is also swelling of the muller cells of the retina.[32]

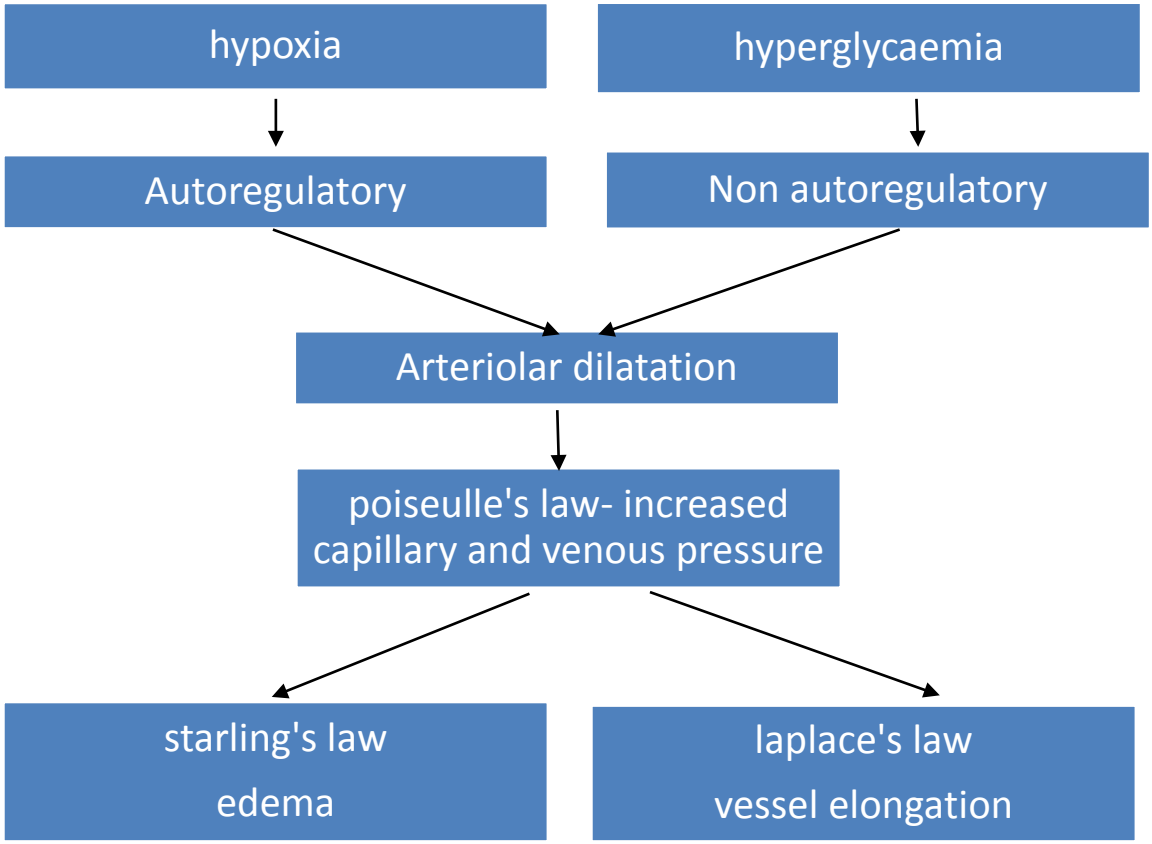
Exudate fluid contains water, protein and lipid material, which gets collected in the outer plexiform layer of the parafoveal region. The water gets reabsorbed leaving behind the lipid material in the outer plexiform layer which is seen as hard exudates during examination.

MECHANISM OF DEVELOPMENT OF DIABETIC MACULAR EDEMA

Physiological factors that lead to the development of macular edema is similar to the factors that cause edema in any other tissue of the body.

As per starlings law of capillary, macular edema occurs whenever there is an increased hydrostatic pressure gradient between capillary and retinal tissue. An increase in intravascular hydrostatic pressure from hypertension or intravascular fluid overload will drive fluid across the vessel wall. In early diabetic macular edema the breakdown of inner blood retinal barrier predominates over the dysfunction of outer blood retinal barrier. In addition auto regulation of blood flow and intrinsic integrity of proteins forming inner blood retinal barrier is also impaired. Anaemia contributes to development of diabetic macular edema by impairing oxygen supply to retina.

FIGURE 5: MECHANISM OF DEVELOPMENT OF DIABETIC MACULAR EDEMA



Autoregulatory arterial dilatation occurs in response to hypoxia and hyperglycamia respectively. As per poiseulle's law pressure of the capillary or vein increases with the increase in radius of the vessel.

According to starling's law whenever there is break in the blood retinal barrier there is movement of water and solutes out of the capillaries leading to macular edema.

As per laplace's law increase in hydrostatic pressure within the vessel lead to both dilatation and elongation of the vessel leading to tortuosity of the vessels.

4. CLASSIFICATION

Diabetic macular oedema is defined as clinically significant macular oedema by ETDRS classification as follows

I. At the centre of the macula, thickening of the retina or within 500 micron

II. Hard exudates at the size of 500 micron at the centre of the macula or if associated with thickening of the adjacent retina.

III. Zones of retinal thickening which is one disc area or larger any part which is within one disc diameter at the centre of the macula.

The most important purpose of this classification is to separate the eyes with Clinically Significant Macular Edema from no apparent retinal thickening or any lipid in the macula.

If the examiner is using direct ophthalmoscopy due to lack of equipment, it may be difficult for giving definitive diagnosis of retinal thickening without stereopsis. The international clinical diabetic macular edema scale is a two-tiered system where initial decision is made on whether retinal thickening is present or not in the posterior pole, followed by second level decision regarding thickening location in relation to macula.

The international clinical diabetic macular oedema disease severity scale(31)

Disease severity level in macular oedema	**Findings observed upon dilated fundus examination**
Diabetic macular oedema Apparently Absent in diabetic retinopathy	No apparent retinal thickening or hard exudates seen in posterior pole
Diabetic macular oedema apparently present in diabetic retinopathy	Some apparent retinal thickening are seen or some hard exudates in posterior pole
If diabetic macular oedema are present, it can be classified as follows:	
Disease Severity Level in macular oedema	Severity Level Findings Observed in dilated fundus examination
Diabetic Macular oedema seen	Edema seen 1. Mild Diabetic Macular oedema with Some retinal thickening or some hard exudates is seen in posterior pole but distant from the centre of the macula 2. Moderate Diabetic Macular Edema Retinal thickening with hard exudates approaching the centre of the macula is seen but not involving the centre 3.Severe Diabetic Macular Edema Retinal thickening along with hard exudates involving the centre of the macula.

Classification based on Fundus Fluorescein Angiography

Although there is decreasing trend towards use of fluorescein angiogram in management of diabetic macular edema, it is desirable to do a baseline FFA in all patients with diabetic macular edema. FFA is especially preferable in cases with disproportionate vision loss compared to clinical picture (e.g. Macular ischemia), in cases with suspicion of neovascularisation, in cases with mixed retinopathy and in patients who are not responding to treatment.

Blankenship et al classified diabetic macular edema based on FFA by counting the number of leakage sites on the fovea 60 seconds after fluorescein injection. The counting was done in a 30 degree photograph centered on the fovea. Eyes with six or fewer leakage sites were classified as focal DME and eyes with seven or more leakage sites were classified as diffuse. Alteration in capillaries distribution of macular area or enlargement of Foveal Avascular Zone is termed as Macular ischemia.

Persistent diffuse macular edema can progress to cystoid macular edema. At the fovea where the structure of muller fibre is weaker, the retina yields leading to formation of larger cysts. Due to necrosis of muller cells cystoid cavities form , which in initial stages present as pseudocysts at the level of inner and outer nuclear layers. The cysts gradually extend towards the inner and outer plexiform layers.

5. PATHOPHYSIOLOGY

Molecular mechanism and pathological changes

Chronic hyperglycaemia is the basic factor which leads to various biochemical pathways which includes polyol pathway, advanced glycation end products formation, PKC-DAG pathway, excessive oxidative stress, increased inflammatory mediation etc which leads to histopathological changes including basement membrane thickening, pericyte loss, capillary occlusion, and neovascularisation. [1]

I. Polyol pathway

Due to excessive intra cellular level of glucose there occurs shunt of the remaining glucose left after saturation of the normal pathway to the aldose reductase pathway.

Glucose is reduced to sorbitol by the enzyme aldose reductase by using NADPH as a co factor. Sorbitol accumulation within the cell leads to the changes in the osmotic gradient which in turn causes cellular damage.

Even though the sorbitol is converted to fructose by sorbitol dehydrogenase with NAD+ as a cofactor this occurs more slowly leading to toxic accumulation of sorbitol with in the cell. [2.]

II. Advanced glycation end products(AGEs) formation

AGE forms due to non enzymatic glycation of intracellular and extra cellular proteins and lipids. AGE formation proportionately increases with duration of hyperglycaemia. [3]

AGE alter the cellular function by two mechanisms

1. Interacting with type IV collagen and inhibiting the lateral association of these molecules into network like structure.
2. Binding of AGE to receptors for advanced glycation end products (RAGE)These mechanism lead to the alteration in the matrix components ultimately leading to basement membrane thickening. [4]

III Oxidative stress/reactive oxygen species formation

Hyperglycaemia state leads to increased production of reactive oxygen species by oxidative phosphorylation and glucose auto oxidation.[5] Brownlee et al have suggested oxidative stress as an "unifying mechanism" that link other biochemical pathways ultimately leading to pathological changes in retina.

IV Protein Kinase C &Diacyl Glycerol Activation.

The proposed increase in activation of intracellular signalling molecule protein kinas C and diacyl glycerol leads to the change in various vascular functions including permeability, vasodilator release, endothelial activation and growth factor signalling.

V Leukostasis

Hyperglycaemia induced glycosylation on surface carbohydrate of leukocytes lead to leukocyte dysfunction.[6] Endothelial dysfunction along with leukocyte dysfunction leads to increased interaction of both the cells leading to leukostasis.

VI Increase in Vascular Endothelial Growth Factor mediators(VEGF mediators)

The various growth factors involved in pathogenesis of diabetic retinopathy are Insulin like growth factor-1 (IGF-1), Transforming Growth Factor Beta-2 (TGF-ß2), Platelet Derived Growth Factors (PDGF), Stromal Derived Growth Factor, Epidermal Growth Factor, Vascular Endothelial Growth Factor (VEGF).[7]

VEGF – isoforms 121, 165, 189, 206 are widely studied among all other factors and their antagonists are being used for treating diabetic macular edema. VEGF promotes angiogenesis and it causes breakdown of blood retinal barrier, and it stimulates the endothelial cell growth anf neovascularisation which in turn increases vascular permeability. The action of insulin like growth factor is also controlled by VEGF.

The functions of VEGF is mediated by two membrane bound tyrosine kinase receptors. The activation of receptors leads to initiation of two pathways namely calcium influx channel pathway and mitogen activating protein kinase signalling pathway. Both pathways lead to breakage of blood reinal barrier and vascular leakage.

VII Renin Angiotensin Aldosterone System (RAAS)

Based on in vitro studies angiotensin 2 is involved in activation of protein Kinase C activation and VEGF signalling thereby aiding neovascularisation. Increased expression of receptors for renin and angiotensin has been reported in retina of proliferative diabetic retinopathy patients.

6. PATHOLOGICAL CHANGES

Pre clinical changes

a. Loss of pericytes
b. Thickening of basement membrane

Clinical changes

a. Formation of micro aneurysms
b. Abnormality in venous calibre
c. Intra retinal micro vascular abnormalities
d. Cotton wool spots
e. Hard exudates
f. Intra retinal haemorrhage
g. Macular oedema

Pericyte loss

Pericytes are present in outer blood vessel wall they are contractile cells responsible for regulation of blood flow.

They are also needed for maintenance of normal growth and repair of the endothelial cells. Loss of pericytes leads to empty dropout spaces in the capillary wall and. it is evident only on histo pathological examination.

Basement membrane thickening

Basement membrane is made primarily of type IV collagen.Thickening of basement membrane occurs proportionately to the level and duration of hyperglycaemia and it can be reversed by good glycaemia control [7]

Basement membrane thickening is associated with decrease in proteoglycan content which in turn leads to membrane permeability and extravasations of intra cellular fluid.

Microaneurysms

Micro aneurysms occurs due to proliferation of out pouching of the capillary endothelium in areas of pericyte loss

They appear as a tiny red dot in the retina during ophthalmic examination size range from 25 to 100 microns, seen in the posterior pole especially temporal to macula

Increase in number of micro aneurysms indicates progression of retinopathy.

Microaneurysms may appear isolated or can be seen as clusters. Leakage from the wall of microaneurysm occur due to defective inner blood retinal barrier which in turn leads to edema of the retina and hard exudate formation.

Types of microaneurysms

1. Background microaneurysms

   These are small lesions that are difficult to see through ophthalmoscopy, but they can be evident by fundus fluorescein angiography as tiny dot hyperfluorescences not increasing in size or intensity. They can disappear and reappear in some other areas.

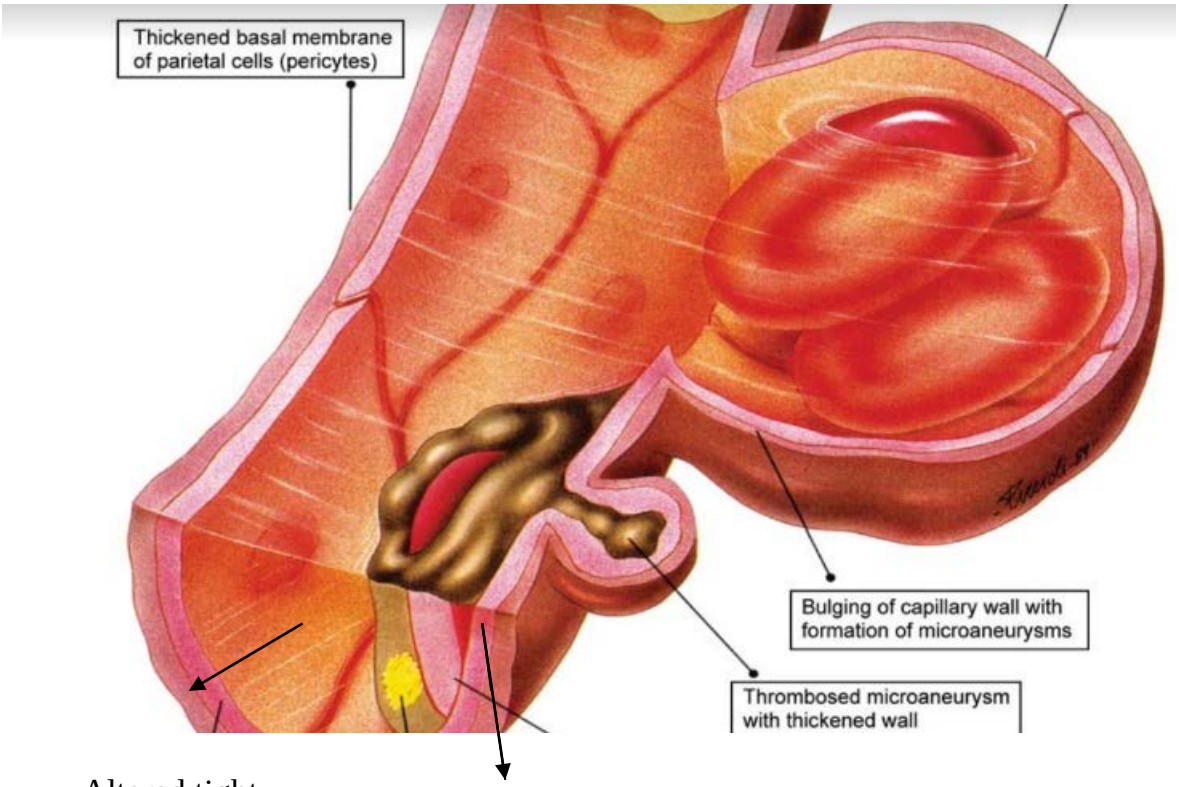
2. Advanced microaneurysms

   These can be seen clearly through ophthalmoscope and they do leak during fundus fluorescein angiography. Due to intact blood flow within microaneurysm they can be seen clearly by OCT angiography.

3. Thrombosed microaneurysms

They appear yellow to white on ophthalmoscopic examination and has irregular walls due to thickening of the walls. During fluorescein angiography they do not fill with dye.

FIGURE 6: SCHEMATIC REPRESENTATION-MICROANEURYSM



Cotton wool spots

Grey semi opaque lesions with feathery edges occurring due to micro infarction of the retinal nerve fibre layer. Can be differentiated from hard exudates because of their irregular margins.

It is also called as cystoid bodies

Intra retinal haemorrhages

Occurs as a result of ruptured micro aneurysms and leaking capillaries

Haemorrhages in inner plexiform, inner nuclear, outer plexiform layer appears as dot and blot haemorrhages because of the arrangements of cellular architecture in this area perpendicular to the retinal surface.

Haemorrhages in retinal nerve fibre layer appear as flame shaped haemorrhages because these fibres are arranged parallel to the surface of the retina.

Venous abnormalities

`Venous dilation, venous bleeding, venous loop formation, occurs as a functional consequence to hyperglycaemia. Due to stasis in the venous circulation, there is delay in the filling of large branches of the vein.

Arteriovenous Shunts

Due to ischaemia shunt may occur between retinal arteries and retinal veins

Venous duplications

Duplications develop when a collateral vein accompanying a vein enlarges and replaces the main branch of the vein.

Venous Meanders and Venous loops

Venous meanders form due to traction of a vein by vitreous and when the meander rotates on itself, due to traction it forms a venous loop.

It is also a reversible change like micro aneurysms return to normal when hyperglycaemia is controlled.

Intra retinal micro aneurysms

IRMA is shunt vessels within the neural retina where there are dilated capillaries due to non perfusion of retina. The dilated capillaries looks wavy and they are located within the neural retina in contrast to new vessels which are situated superficially. They are associated with retinal edema and they do not cause haemorrhage into the vitreous.

It is made of endothelium with thickened membrane and reduced number of pericytes.

Circinate Hard exudates

Lipoprotein deposits in the outer plexiform layer that appear around intra retinal vascular abnormalities forming a star shaped or circinate pattern. The precipitate forms a margin between the normal and edematous retina.

Proliferative diabetic retinopathy

Ischemia of retina leads to increase vascular endothelial growth factor expression and this causes formation of new vessels. These new vessels are usually found on the margin of the ischemic areas. These new vessels have only single layered fragile wall formed by endothelium. They easily rupture leading to pre-retinal or vitreous haemorrhages. In fundus fluorescein angiography they present as leakage that increase in size and intensity. Whenever there is presence of neovascularisation of the disc and or neovascularisation elsewhere or there is clinical evidence of vitreous or pre retinal haemorrhages super imposed on non proliferative changes it is termed as proliferative diabetic retinopathy.

NVD – new vessel on the disc or within one disc area of the optic nerve head

NVE – new vessel growth on the retina in location greater than one disc area from the optic nerve head is termed as new vessel else where

These new vessels can occur in anterior chamber or angle also leading to neo vascular glaucoma.

Pan retinal photocoagulation can lead to regression of these fragile new vessels.

7. RISK FACTORS

The reported risk factors for the occurrence of diabetic macular oedema are duration of diabetes, dyslipidaemia, proteinuria and micro albuminuria, increased glycated haemoglobin (HbA1c), hypertension, socioeconomic status, elderly age group, and increasing severity of diabetic retinopathy.

1. DURATION OF DIABETES

Duration of Diabetes is an important predictor of Diabetic retinopathy in both Type 1 and Type 2 Diabetes mellitus patients. In Wisconsin Epidemiological Study of Diabetic Retinopathy, increase in prevalence of diabetic retinopathy was documented in patients with increasing duration of diabetes.

2. HYPERGLYCEMIA

The relationship between glycaemic control and all the vascular complications of diabetes was assessed by the landmark trials, the Diabetes Control and Complication Trial and the United Kingdom Prospective Diabetes Study. Patients with higher glycated hemoglobin values were shown to have a higher risk for developing retinopathy. With good control of having glycosylated haemoglobin within 7gms% the progression of diabetic retinopathy can be delayed.

One of the most important predictive factors for diabetic retinopathy is the level of glycaemic control. The glycaemic control has become the most important predictive factor for development of retinopathy.

3. HYPERTENSION

Hypertension is a common comorbid condition in patients with diabetes.[20] According to the findings of Wisconsin Epidemiological Study of Diabetic Retinopathy 17% of patients with type 1 diabetes had hypertension at baseline, and 25% of patients developed hypertension eventually in the following 10 years.

Impairment of retinal vascular autoregulation in response to elevated blood pressure may play a role, based on observations that diabetic patients with hypertension appear to have an impaired ability to regulate retinal blood flow when compared with non-diabetic patients.[16]Hypertension can result in endothelial damage in the retinal vasculature, and there is an increase in expression of vascular endothelial growth factor and its receptors in diabetic patients. Hypertension is an independent risk factor influencing the onset of retinopathy irrespective of the duration of diabetes mellitus and glycaemic control.

As per United Kingdom Prospective Diabetes Study, hypertension control with captopril an Angiotensin Converting Enzyme Inhibitors or atenolol a beta blockers may delay the progression of diabetic retinopathy even in normotensive individuals. The patients in tight BP control group were less likely to develop macular edema and their need for laser photocoagulation is also less when compared to conventional BP control group.

4. HYPERLIPIDEMIA

As evidenced by various epidemiological studies, dyslipidemia is an important risk factor for retinopathy and Clinically Significant Macular Edema. The association of higher total serum cholesterol with retinal hard exudates is found in both the younger and the older onset groups with type 2 diabetes. The patients with higher levels of triglycerides, low-density lipoproteins, and very low-density lipoproteins at baseline were associated with an increased risk of hard exudates and decreased visual acuity.

According to (FIELD study) Fenofibrate Intervention and Event lowering in Diabetes ,lipid lowering therapy may be beneficial for patients with diabetes and dyslipidemia both for its effects on cardiovascular morbidity and for its possible effects on retinopathy.

Oral atorvastatin therapy in patients with type 2 diabetes with dyslipidemia can reduce the severity of hard exudates and sub-foveal lipid migration in clinically significant macular edema and could be an important adjunct in the management of clinically significant macular edema. [24]

5. EXOGENOUS INSULIN

Exogenous insulin has been suggested as a possible cause of both macrovascular and microvascular disease, including retinopathy, in people with type 2 diabetes. But in Wisconsin Epidemiolosical Study of Diabetic Retinopathy, there was no association found between the amount or type of exogenous insulin used and the presence of diabetic retinopathy.

6. PROTEINURIA AND NEPHROPATHY

Diabetic retinopathy is closely linked with nephropathy, because of the fact that both frequently coexist in diabetic patients, as both are microangiopathies having common predisposing factors and pathogenic mechanisms. For example longer duration of diabetes, hyperglycemia and hypertension all are well-established risk factors for both retinopathy and nephropathy.

The presence of gross proteinuria at baseline was associated with a 95% increased risk of developing macular edema in the Wisconsin Epidemiologic Study of Diabetic Retinopathy 14-year follow-up study.

7. CIGARETTE SMOKING AND ALCOHOL

As per cardiovascular risk factor studies cigarette smoking is a known risk factor for atherosclerotic diseases while moderate alcohol consumption has been suggested to be cardioprotective. However, epidemiological studies, including the WESDR, did not found any pattern of association between either smoking or alcohol consumption and risk of retinopathy.[23]

8. BODY MASS INDEX

The association between obesity and diabetic retinopathy has been investigated in several studies. Some studies have documented a relationship between larger body mass index (BMI) and risk of retinopathy, whereas some other studies proved otherwise probably due to the fact that the patients in severe phase of diabetes belong to lean BMI .

9. PHYSICAL INACTIVITY

Exercise and physical activity may have a positive effect in reducing the risk of diabetic complications, by direct action of lowering blood glucose levels and increasing insulin sensitivity or by indirect action via improved cardiovascular function like increasing high density lipoprotein (HDL), lowering risk of hypertension.

10. ANAEMIA

Anaemia is an important factor that is thought to worsen Diabetic Macular Edema.[25] Epidemiological studies have shown that Hb levels <12 g/dL result in doubling of the risk of DR. Systemic erythropoietin therapy appears to improve DME, likely through an increase in haemoglobin levels. This results in increased oxygenation of the retina and, ultimately, less ischemia induced VEGF production. Another possible mechanism is via the neuroprotective role of erythropoietin on the retina.

Friedman et al has conducted a preliminary clinical trials by injecting erythropoietin in 1000 anaemic diabetic subjects with nephropathy to assess the effect of increase in red cell mass on the well-being of the patient and the course of renal function decline of those patients. The study has substantiated that pseudohypoxia due to hyperglycamia may be implicated in pathogenesis of diabetic neuropathy, nephropathy, muscular dysfunction and retinopathy.[26]

8. MANAGEMENT

1. Primary prevention

Primary prevention is avoiding the risk factors that are implicated in the development of the disease. Good metabolic control is the main factor to be focused in primary prevention. Regular exercise, diabetic diet, avoidance of sedentary life style, maintaining blood parameters within normal range by appropriate drugs are the main factors in primary prevention.

2. Secondary prevention

Aims at reducing the severity of the disease by timely intervention .

Before the advent of Anti-VEGF, focal/ grid laser is the main standard of care for CSME.

In ETDRS study, in eyes with CSME focal or grid laser reduced the vision loss when compared to observation.

Standard spot size is 50- 100µm and burn duration is 0.1 second. Argon Green laser with wavelength 514 nm is applied between 500µm and 3000µm from the centre of the macula. Each burn are separated by one burn width. End point is barely visible light grey outer retinal colour change.

Grid pattern is used when there is diffuse leakage, to place uniformly spaced burns of size 50 – 200 microns at the level of retinal pigment epithelium. When the leakage is intense each burn are separated by one burn width for less severe leakage

the burns are placed slightly farther away. Duration is 0.1 sec or less until there is barely visible light grey discolouration of outer retina.

Laser sessions are repeated until all micro aneurysms are treated adequately or till resolution of retinal thickness to normal range.[33]

Laser photocoagulation has poor outcome in patients with

1. Macular ischemia, extensive capillary non perfusion area in perifoveal region.
2. Hard exudates at the foveal area.

Mechanism of action of laser photocoagulation

Effect of laser treatment is by thermal damage at the level of the RPE.

Direct mechanism

Direct thrombosis due to absorption of light by haemoglobin resulting in closure of micro aneurysm .

Indirect mechanism

Laser induced destruction of retinal photoreceptors, RPE and chorio capillaries leading to direct diffusion of oxygen from chorio capillaries to the inner retina via the laser scar relieving the retinal hypoxia.

The other mechanisms by which laser photocoagulation acts include

- Photocoagulation debridement of dysfunctional retinal pigment epithelium and replacement with healthy retinal pigment epithelium thereby enhancing outer retinal barrier function.

- Stimulation of Vascular endothelial proliferation resulting in restoration of inner blood retinal barrier.
- Reduction in total surface area of the leaking vessels.

The possible adverse effects of photocoagulation are inadvertent macular burns, paracentral scotomas due to coalescence of laser scar in the macular area, transient loss of vision due to increase in oedema, diminished dark adaptation, sub retinal fibrosis, choroidal neovascularisation.

As per the recommendations of Early Treatment Diabetic Retinopathy Study, focal laser is indicated for focal leakage where laser is directed at specific areas of focal leakage. For diffuse leakage grid pattern of burns is applied to areas of leakage or to areas of non-perfusion.

Eventhough the recovery of reduced vision is unlikely with laser treatment the goal of laser photocoagulation is to achieve moderate improvement or stabilisation of the existing vision.

INTRA VITREAL ANTI-VEGF

VEGF-A is a 45-kDa homodimeric glycoprotein, it has 4 human isoforms namely 121, 165, 189 and 206, the number denotes the number of amino acids contained in the secreted protein.[28]

VEGF- 165 is the primary mediator of pathologic vascularisation

Anti-VEGF agent is used to inhibit over expression of vascular endothelial growth factors as a consequence of hyperglycaemia induced oxidative damage

Intra-vitreal Anti-VEGF aptamer

Pegaptanib sodium (Macugen) – pegylated aptamer that binds to VEGF-A165 isoform similar to antigen antibody reaction

Intravitreal Anti-VEGF

Bevacizumab (AVASTIN)

Humanised monoclonal full length antibody that binds with all isoforms of anti-VEGF

Administered in a dosage of 1.25mg in 0.05ml at 4-6 weeks interval for 3 doses

Ranibizumab (LUCENTIS)

Humanised monoclonal antibody fragment much smaller than its parent molecule bevacizumab and it binds with all four isoforms of VEGF.

Dosage is 0.5mg per 0.05ml once in every month for 3 months

VEGF trap (EYLEA- Aflibercept)

Fusion protein that binds and neutralises VEGF and also placental growth factor.

Dosage is 2mg (0.05 ml) every 4 weeks for first 3 months followed by once in 2 months for 2 years

Pegpleranib – FOVISTA

A pegylated aptamer with Anti-PDGF function is used in combination with Anti- VEGF agents.

Intra-vitreal corticosteroids

Indicated for chronic unresponsive macular oedema

1. Steroids acts by inhibiting gene expression of vascular endothelial growth factor and pro-inflammatory genes.
2. Inhibition of phospholipase A2 pathway
3. Reducing expression of Matrix Metalloproteinases (MMPs).

Corticosteroid Implants

1. Dexamethasone implant (Ozurdex)
2. Triamcinolone acetonide
3. Fluocinolone acetonide (Iluvein, Retisert)

Other newer drugs under clinical trials

1. Infliximab – TNF-α inhibitor
2. Bevasiranib – Small interference RNA
3. Sirolimus a macrolide compound – subconjunctival injection is under phase 2 clinical trials
4. Prinomostat – Matrix Metalloproteinase Inhibitor
5. Ruboxistaurin mesylate – Protein Kinase C – β1/2 inhibitor.[29]
6. Candesartan – Angiotensin Receptor blocker inhibitor
7. Algebrium – Advanced glycation Endproduct crosslink breaker
8. Sorbinil – Aldose Reductase Inhibitor

Surgical management

Surgical management is needed in patients with taut posterior hyaloids or if associated with epiretinal membrane. The recommended surgical treatments are Pars Plana Vitrectomy and Internal Limiting Membrane or Epiretinal membrane peeling.

STEPS OF MANAGEMENT OF MACULAR EDEMA

1. Complete ocular examination
2. Adequate metabolic control
3. To exclude other treatable causes of macular edema
4. Laser photocoagulation
5. Follow up and reassessment
6. Other treatment with pharmacologic agents (Anti- vascular endothelial growth factors and steroids)

9. REVIEW OF LITERATURE

In a cross sectional study conducted by PK Rani in 198 diabetic retinopathy screening camps were conducted in which 26,519 self reported rural population were participated.

The prevalence of diabetic retinopathy was found to be 17.6%. Male gender was positively associated with presence of retinopathy but not with the severity of retinopathy.

Lean BMI was associated with diabetic retinopathy. Systolic blood pressure and insulin treatment showed positive association with diabetic retinopathy.

The Chennai Urban Rural Epidemiology Study (CURES) which was a population based study and it had 17.6% prevalence of diabetic Retinopathy. Prevalence was more in men than in women. [8]

For every five year increase in duration of diabetes increases the risk of having Diabetic retinopathy increases by 1.89 times. Every 2% elevation of glycated haemoglobin (HbA1c) the risk of having Diabetic retinopathy increases by 1.7 times. With increase in duration of disease the severity of diabetic retinopathy also increases.

The patients with proteinuria had more prevalence of diabetic retinopathy.

In a study conducted in Australia by rehab benarous et al., proved that serum lipid levels are independently associated with clinically significant macular edema, but not associated with diabetic retinopathy;

In a study conducted in multiethnic population in Malaysia, total cholesterol and glycated haemoglobin had positive association with clinically significant macular oedema.

Rajiv raman et al in Shankara Nethralaya Diabetic Retinopathy Epidemiology and Molecular Genetics Study (SN DREAMS- III report -2) found prevalence of diabetic retinopathy in rural population as 10.4%.

It also stated duration of diabetes to be a strongest predictor of diabetic retinopathy. The other factors that had statistically significant association with diabetic retinopathy were male gender, insulin treatment, and longer duration of diabetes, poor glycaemia control and systolic hypertension.

A cross sectional study from Turkey found prevalence of diabetic macular oedema to be 15.3%. The statistically significant factors associated with prevalence of clinically significant macular oedema were male gender, longer duration of diabetes, alcohol consumption, nephropathy, neuropathy, diabetic retinopathy severity, insulin treatment and previous history of intraocular surgery. Treatment with anti-hyper lipidaemic drugs and high levels of high density lipoprotein had negative association with clinically significant macular oedema.

Pradeep venkatesh et al documented that patients with clinically significant macular edema had higher percentage of nephropathy irrespective of degree of the severity of retinopathy

There existed a significant correlation between nephropathy, neuropathy and macrovascular complications with initial grades of diabetic retinopathy.

Wisconsin Epidemiological Study of Diabetic Retinopathy had elucidated the relation of serum cholesterol to diabetic retinopathy and hard exudates.

Early Treatment Diabetic Retinopathy Study had proved that the patients with increased levels of total cholesterol and serum low density lipoprotein were more likely to have retinal hard exudates.

According to United Kingdom Prospective Diabetes study (UKPDS) triglyceride and Low Density Lipoprotein levels were not related to severity of retinopathy. Higher High Density Lipoprotein levels were associated with more severe retinopathy , but did not offered a valid explanation.

ARICS – The Atherosclerosis Risk in communities Study also Documented positive association between plasma LDL and cholesterol level.

According to The Cardiovascular Health Study retinopathy was associated with higher average systolic blood pressure.

Diabetes Control and Complication Trial demonstrated decreased rate of development of diabetic retinopathy by reduction of HbA1C to 7% in type 1 Diabetes Mellitus patients.

PART – II

10. AIMS AND OBJECTIVES

To evaluate the association of systemic risk factors with clinically significant macular oedema in type 2 diabetes mellitus patients

OBJECTIVES

1. To analyse the association of systemic risk factors with clinically significant macular edema in type 2 diabetes mellitus patients
2. To assess the association of risk factors with specific types of clinically significant macular edema.
3. By managing the risk factors appropriately, the vision loss due to clinically significant macular edema can be avoided.

11. MATERIALS AND METHODS

STUDY DESIGN

A hospital based cross sectional study conducted between October 2017 and September 2019.

METHODOLOGY

All patients of type 2 diabetes mellitus with clinically significant macular edema who attended ophthalmology OPD between October 2017 and September 2019 and within inclusion criteria were included in the study after obtaining written consent.

INCLUSION CRITERIA

I. All patients of either sex with Type 2 DM with clinically significant macular oedema as defined in ETDRS classification who presented in ophthalmology outpatient department were included in the study after getting informed consent.

EXCLUSION CRITERIA

I. Patients who have undergone cataract surgery, glaucoma surgery, vitreo-retinal surgery in the past 3 months,

II. Patients who have undergone retinal laser photocoagulation or who had intraocular injection in the past 3 months

III. Patients with hazy media preventing adequate visualisation of the Fundus

IV. Patients with Type 1 Diabetes Mellitus or Gestational diabetes mellitus

V. Patients who had pre-existing renal disease

VI. Patients who are already on hemo dialysis or peritoneal dialysis

METHOD OF COLLECTION OF DATA

All patients included in the study were subjected to complete ophthalmologic examination by assessing the visual acuity with Snellen chart, Amsler's grid test, slit lamp examination, Fundus examination with direct ophthalmoscope, indirect ophthalmoscope, and slit lamp bio microscopy with +90D lens.

Clinical examination

Blood pressure measurement- Systolic BP >140 mmhg, Diastolic BP >90 mmhg

Body Mass Index: weight (kg)/height in metre square.

Underweight- <18.50

Normal- 18.50-24.99

Overweight – >25.00

Obese - >30

Note: Based on WHO criteria, BMI is age independent and the same for both sexes

Investigations:

- Blood sugar- Fasting ->126 mg/dl ,Postprandial ->200 mg/dl or Random blood sugar >200mg/dl
- ECG- evidence of previous myocardial infarction or ischemic changes (elevation/depression of S-T segment, inversion of T-wave) on ECG supported by clinical history and/or echocardiogram, or a history of cardiovascular surgery or angioplasty for IHD.

- Lipid profile-Fasting total serum cholesterol level >240mg/dl, serum triglyceride ->200mg/dl, serum LDL->190mg/dl, serum HDL<40mg/dl.
- Nephropathy: Urine albumin>1+(30mg/dl indicating gross proteinuria) or blood urea ->40 mg/dl , serum creatinine >1.5mg/dl
- Anaemia- haemoglobin <12 gm% in females ,<13 gm% in males
- HbA1c-Normal range4.2-6.2%, Good control-6.3-6.8%, Fair control-6.9-7.6%, Poor control >7.6%.

Eye Examination:

- Visual acuity testing with snellen chart
- Slit lamp examination
- Amsler's grid test
- Dilated Fundus examination with a direct ophthalmoscope, indirect ophthalmoscope.
- Slit lamp bio microscopy with +90 D lens
- Fundus Photography .
- Fundus Fluorescent Angiography (FFA)

FFA is done in all patients with clinically significant macular edema after ensuring stable cardiovascular status and normal renal function tests . FFA is performed after obtaining informed consent. After securing intravenous line preferably in cephalic vein of right arm, the patient is seated comfortably. Canon CF1 digital retinal camera is used for taking photograph of fundus. At first fundus photography and red free photos were taken. After injecting 3 ml of 20% sodium

fluorescein dye slowly over 5-10 seconds series of photographs were taken over 10 minutes. The pictures were interpreted for presence of early or late hyper fluorescence, leakage and staining patterns.

Angiographic phases in FFA

The choroidal phase

It is pre-arterial phase typically occurs 9-15 seconds after dye injection, longer in patients with poor general circulation. A cilioretinal artery if present will fill at this time as it is derived from posterior ciliary circulation.

The arterial phase

A second later than the onset of choroidal fluorescence, shows retinal arteriolar filling and continuation of choroidal filling.

The arteriovenous phase / Capillary phase

Shows complete filling of the arteries and capillaries with early laminar flow in the veins, in which the dye stains the venous wall at first leaving an axial hypofluorescent strip. This phenomenon reflects the initial drainage of posterior pole capillaries filling the venous margins and also denotes the faster plasma flow adjacent to the vessel walls where cellular concentration is low.

The venous phase

Laminar venous flow progress to complete filling with late venous phase featuring reducing arterial fluorescence The maximal perifoveal capillary filling

occurs around 20-25 seconds and the first pass of fluorescein in generally completed by approximately 30 seconds.

The Late recirculation phase

Demonstrates the effect of continuous recirculation and elimination of the dye.The dye is absent from the retinal vasculature after 10 minutes.

The normal dark appearance of fovea is caused by three factors:

1. Absence of blood vessels in the Foveal Avascular Zone.
2. Blockage of background choroidal fluorescence due to high density of xanthophyll at the fovea.
3. Blockage of background choroidal fluorescence by the RPE cells at the fovea. RPE cells at the foveal region are taller and contain more lipofuscin pigments than other areas.

Hyperfluorescence

1. Autofluorescence

   Autofluorescent compounds absorb bluelight and emit yellow green light in a similar fashion to fluorescein but in more weaker amount. The classical autofluorescent lesions are optic nerve head drusen and astrocytic hamartoma.

2. Pseudofluorescence

   Non fluorescent reflected visible light prior to fluorescen injection. It is more evident when filters are wearing out.

3. Increased fluorescence

   Enhanced visualisation of normal fluorescein density

4. A window defect

   Caused by atrophy or absence of retinal pigment epithelium in atrophic type of age related macular degeneration It is characterised by very early hyper fluorescence that increase in intensity but does not change in size or shape.

5. Pooling

   Pooling of the dye in anatomical space happen due to breakdown of the outer retinal barrier that is RPE tight junctions

6. Leakage

   Early hyper fluorescence that increase in both size and intensity with time.It occurs due to breakdown of inner retinal barrier. Examples are cystoid macular edema, papilledema

7. Staining

   Prolonged retention of dye in cases of drusens, fibrous tissue, exposed sclera and normal optic disc.Seen in later phases of angiogram after the dye has left the choroidal and retinal circulation.

Hypofluorescence

Absence or reduction of fluorescence may be due to optical obstruction of normal fluorescence or due to inadequate perfusion of tissue leading to filling defects

1. Masking of retinal fluorescence

   Preretinal lesions like blood will block all fluorescence

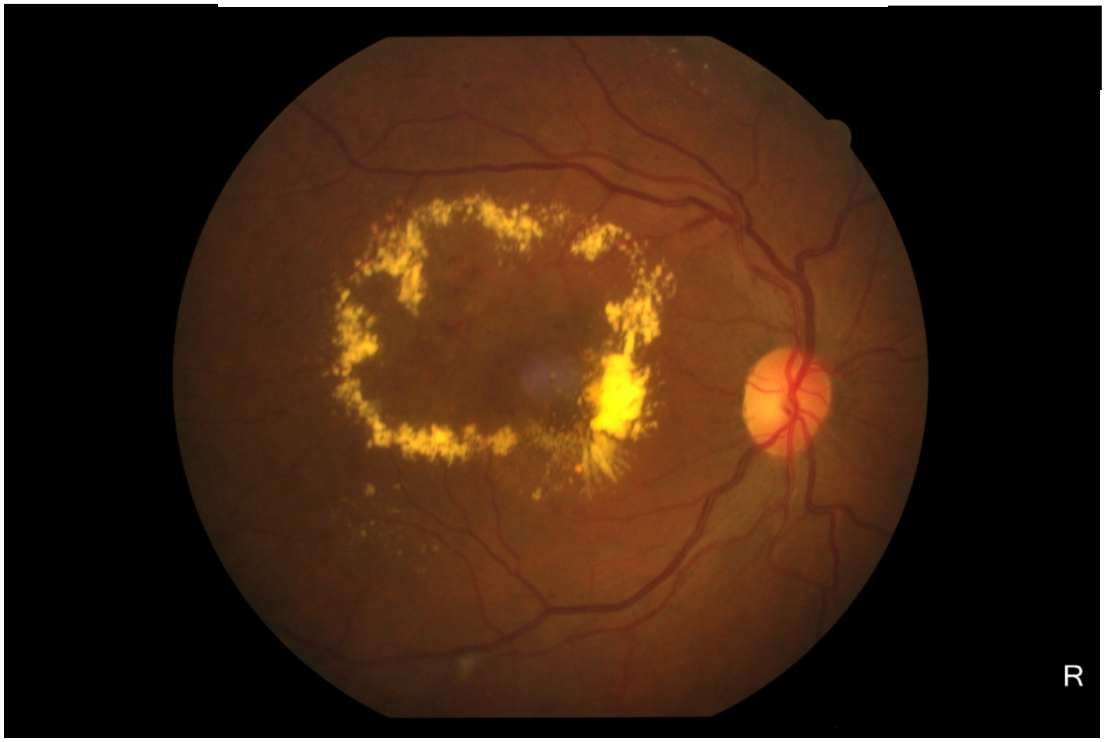
2. Masking of background choroidal fluorescence

   There will be persistence of fluorescence from superficial retinal vessels

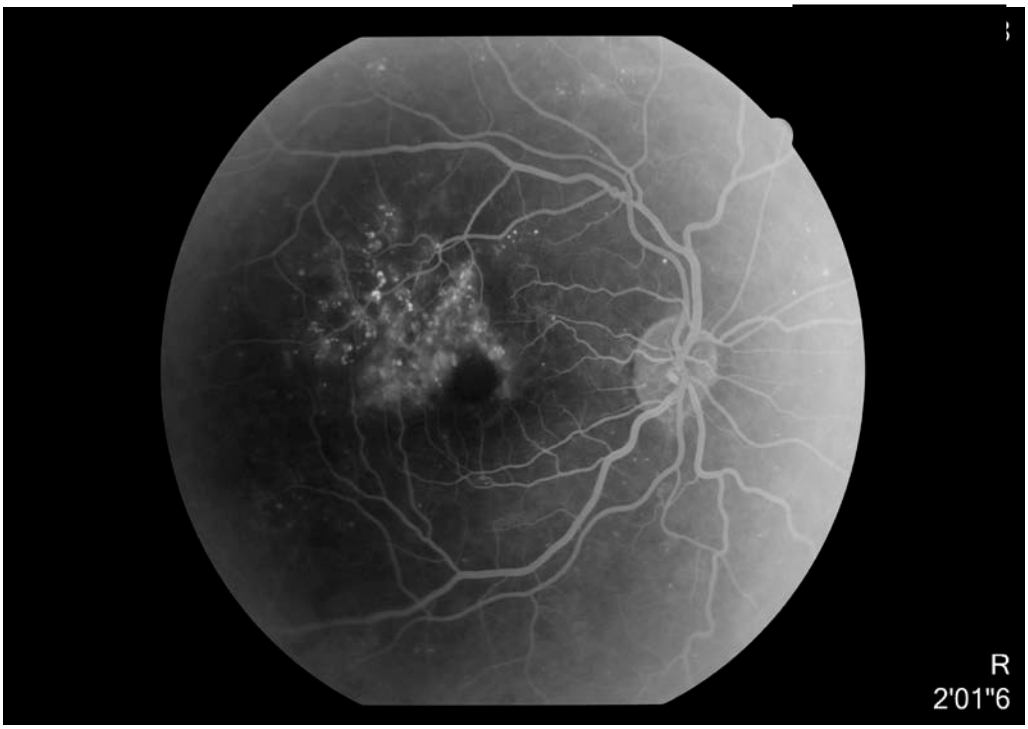
   Examples are deep retinal lesions like intraretinal haemorrhages and dense exudates, subretinal or sub Retinal Pigment Epithelial lesions like blood, Increased densityof the retinal pigmrnt epithelium as in congenital hypertrophy, choroidal lesions like naevi.

3. Filling defects may result from, vascular occlusion of veins, arteries or capillaries (capillary drop out) or the choroidal circulation. Fluorescein angiography may be sometimes useful in demonstrating optic nerve head filling defects as in anterior ischaemic optic neuropathy. Loss of vascular bed as in myopic degeneration and choroideremia can result in filling defects

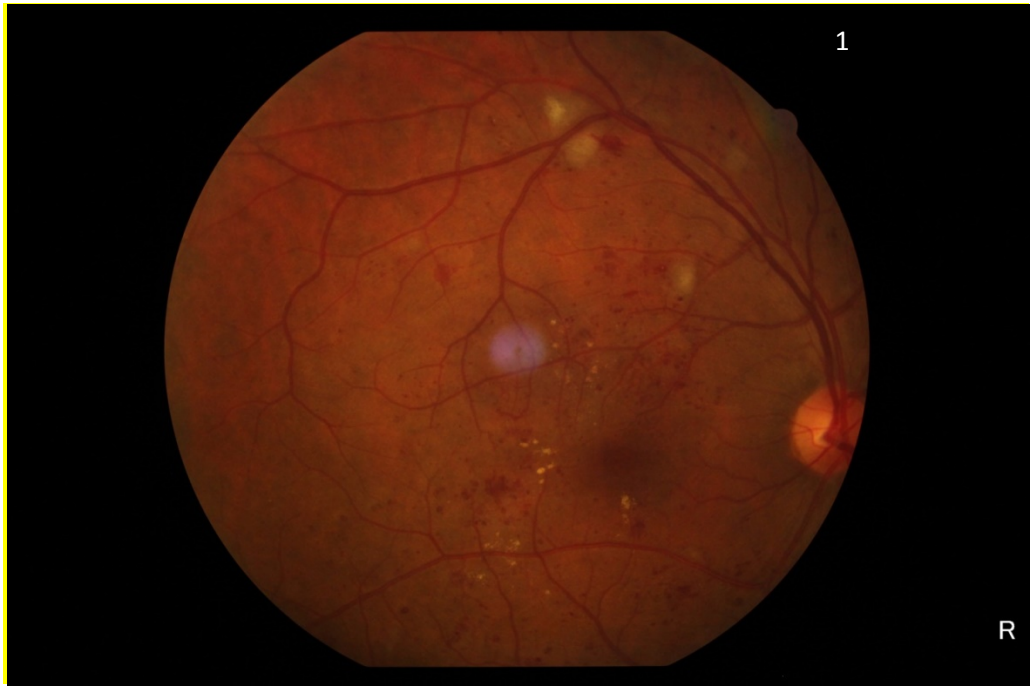
FUNDUS PHOTO – RIGHT EYE CIRCINATE RETINOPATHY



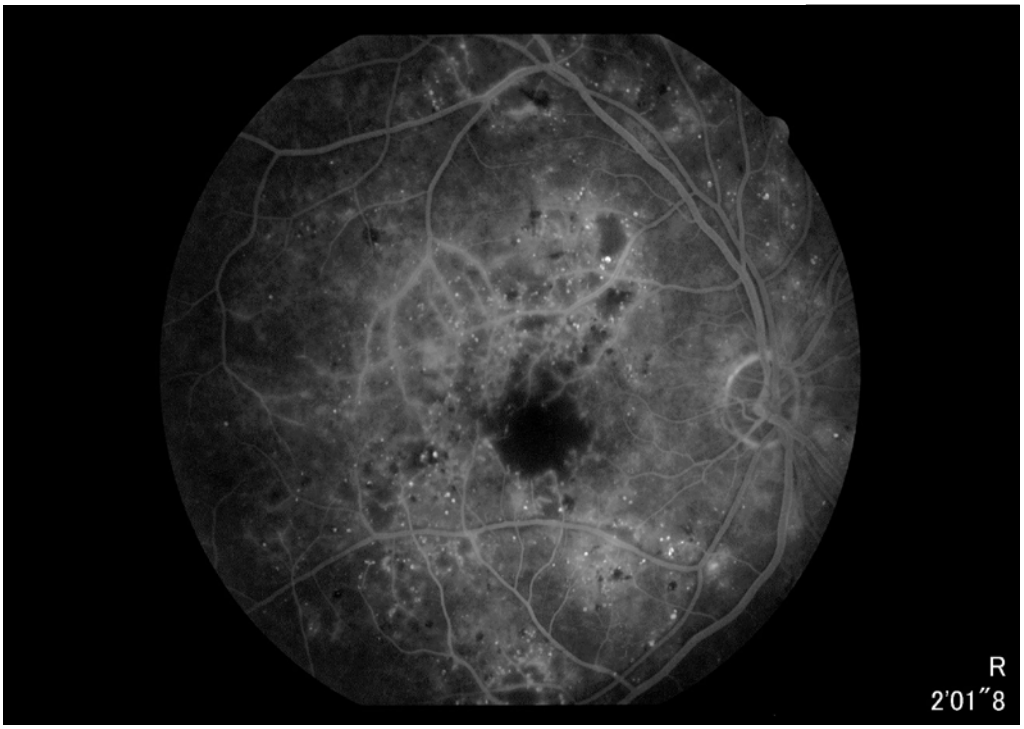
FUNDUS FLUORESCEIN ANGIOGRAPHY- FOCAL LEAKAGE PATTERN IN MACULAR AREA.



FUNDUS PHOTOGRAPHY – Proliferative Diabetic Retinopathy with Clinically Significant Macular Edema

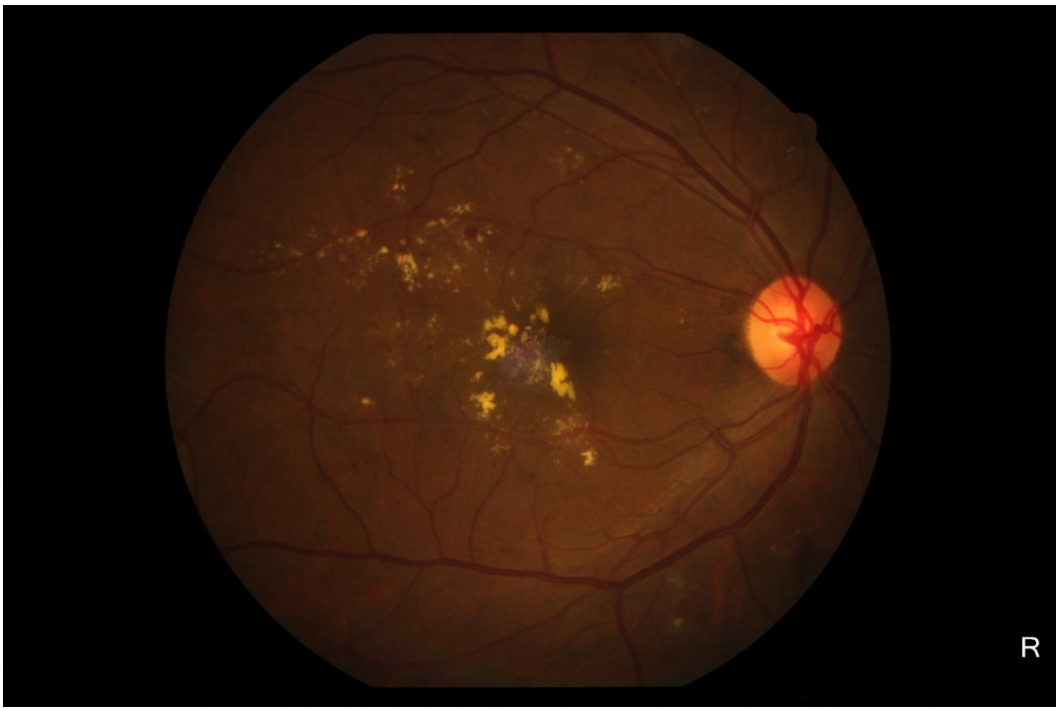


FFA showing capillary non perfusion area in macular area suggestive of macular ischaemia

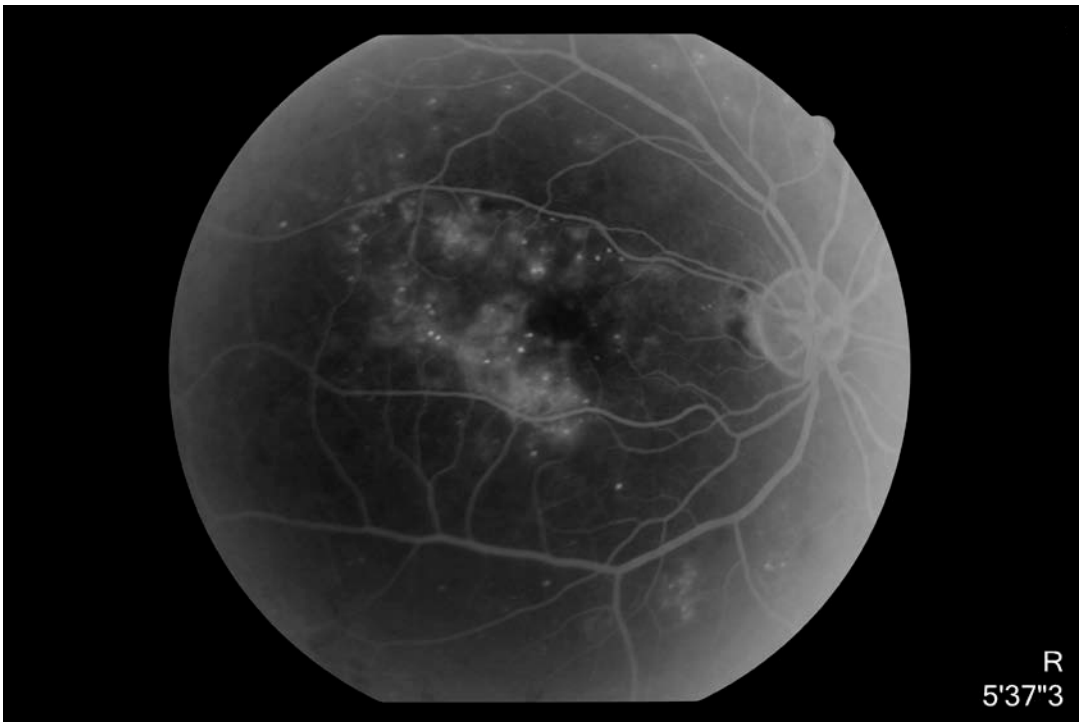


FUNDUS PHOTOGRAPHY

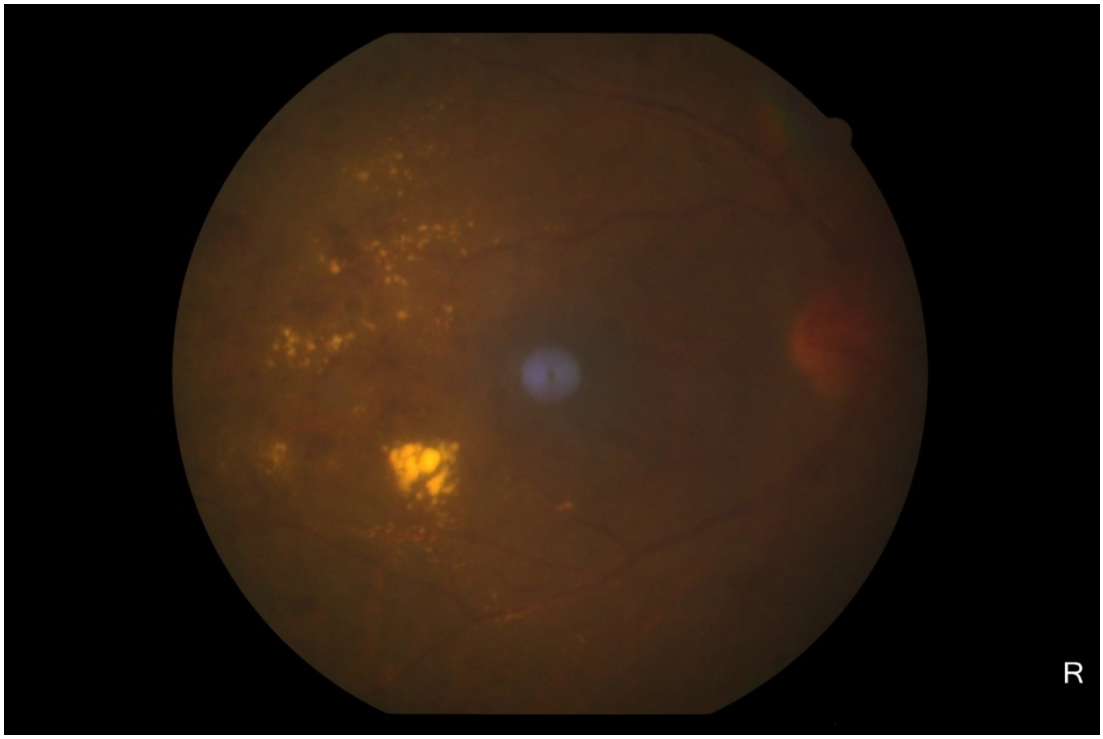
RE – SEVERE NON PROLIFERATIVE DIABETIC RETINOPATHY WITH CLINICALLY SIGNIFICANT MACULAR EDEMA



FUNDUS FLUORESCEIN ANGIOGRAPHY - FOCAL MACULOPATHY

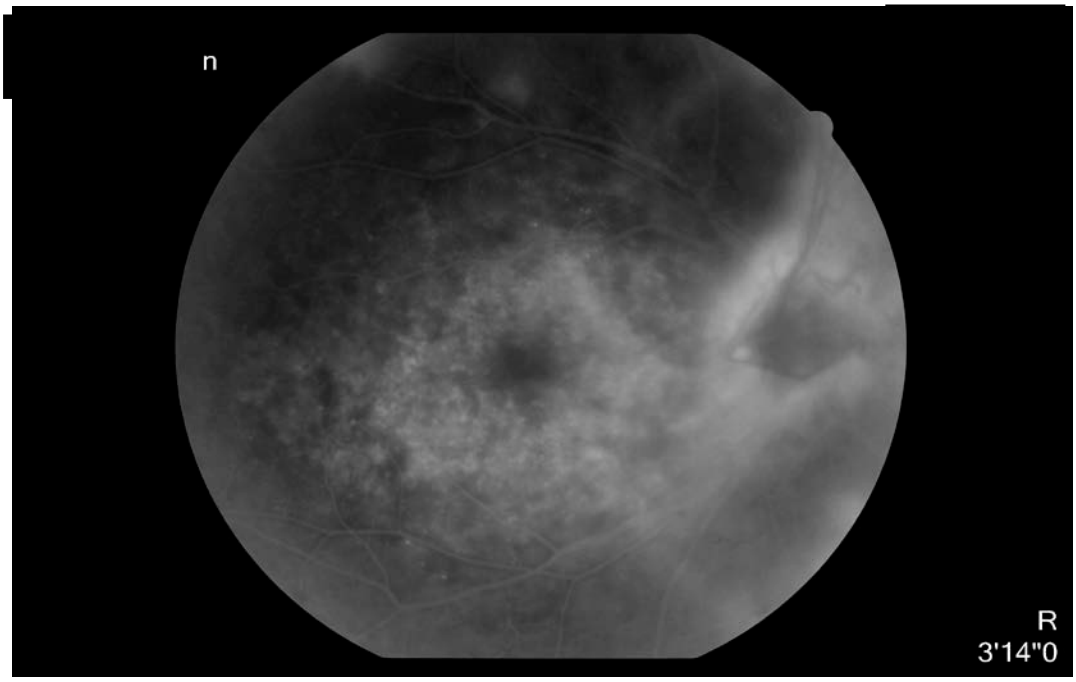


FUNDUS PHOTOGRAPHY- SEVERE NPDR WITH CSME

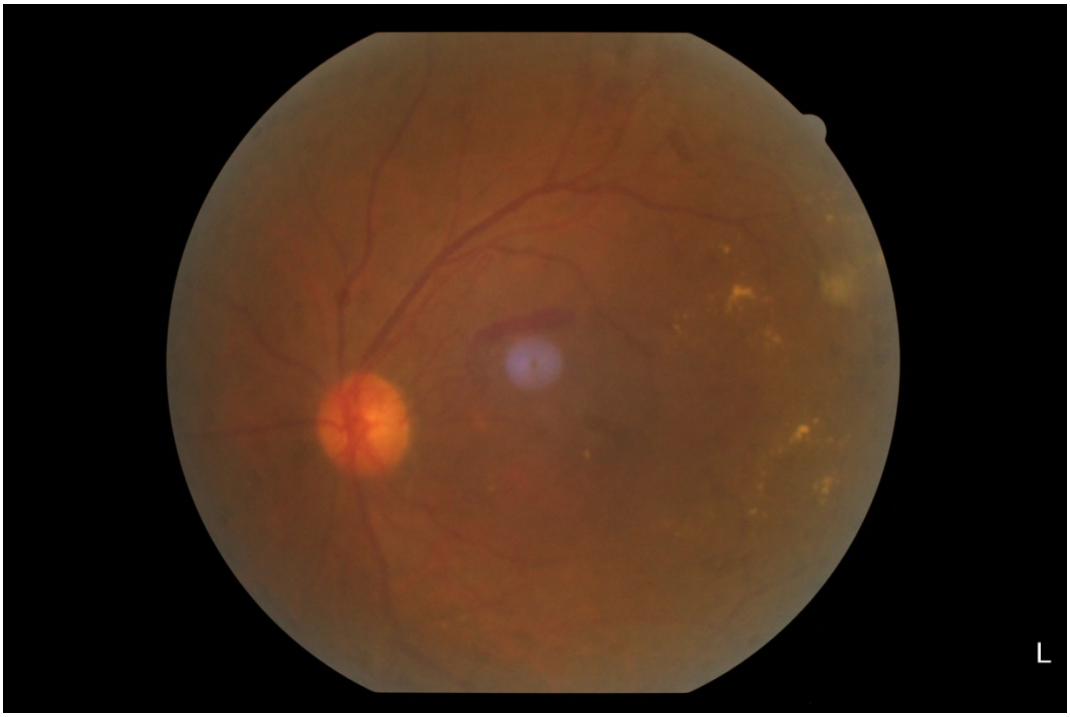


FFA PHOTOGRAPHY- DIFFUSE MACULOPATHY and NVD

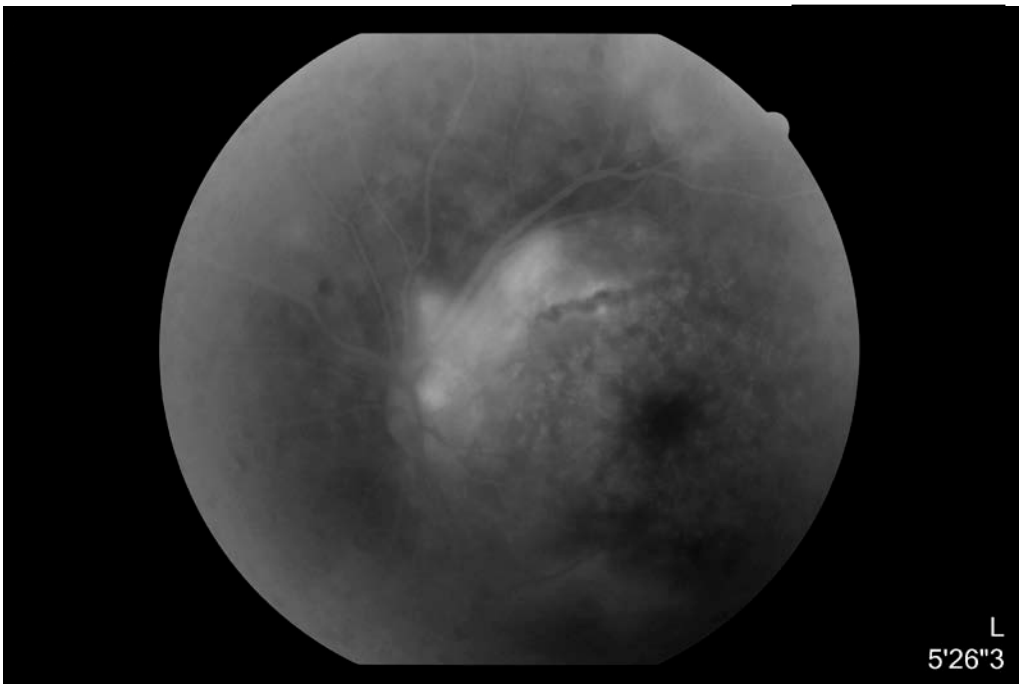
Description – diffuse pattern of leakage in macular area suggestive of diffuse maculopathy and late leak in disc suggestive of new vessels over the disc.



FUNDUS PHOTOGRAPHY- PDR with CSME



FFA PHOTOGRAPHY- DIFFUSE CSME/ late leakage supeotemporal to diac suggestive of new vessels over the disc.



12. OBSERVATION AND ANALYSIS

The collected data were analysed with IBM.SPSS statistics software 23.0 Version.To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significance in categorical data Chi-Square test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used. In both the above statistical tools the probability value 0.05 is considered as significant.

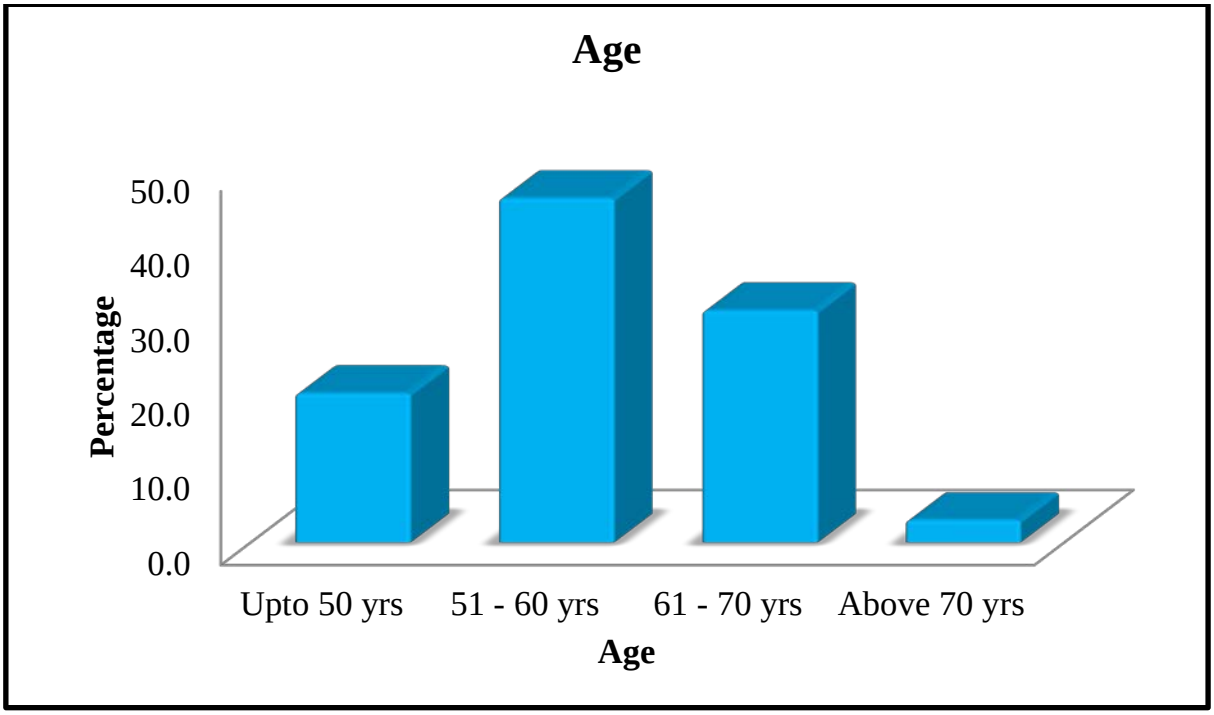
AGE DISTRIBUTION OF STUDY POPULATION

Age group of the study population range from 40 years to 75 years, with mean age of 57.3 years with standard deviation of 7.55. CSME occurrence was higher in51-60 years of age which comprises 46 percentage of study population and the next higher occurrence in the age group of 61 to 70 years of age.

Table 1 : AGE DISTRIBUTION

Age		
	Frequency	**Percent**
Up to 50 yrs	20	20.0
51 - 60 yrs	46	46.0
61 - 70 yrs	31	31.0
Above 70 yrs	3	3.0
Total	100	100.0

Diagram 1 AGE DISTRIBUTION



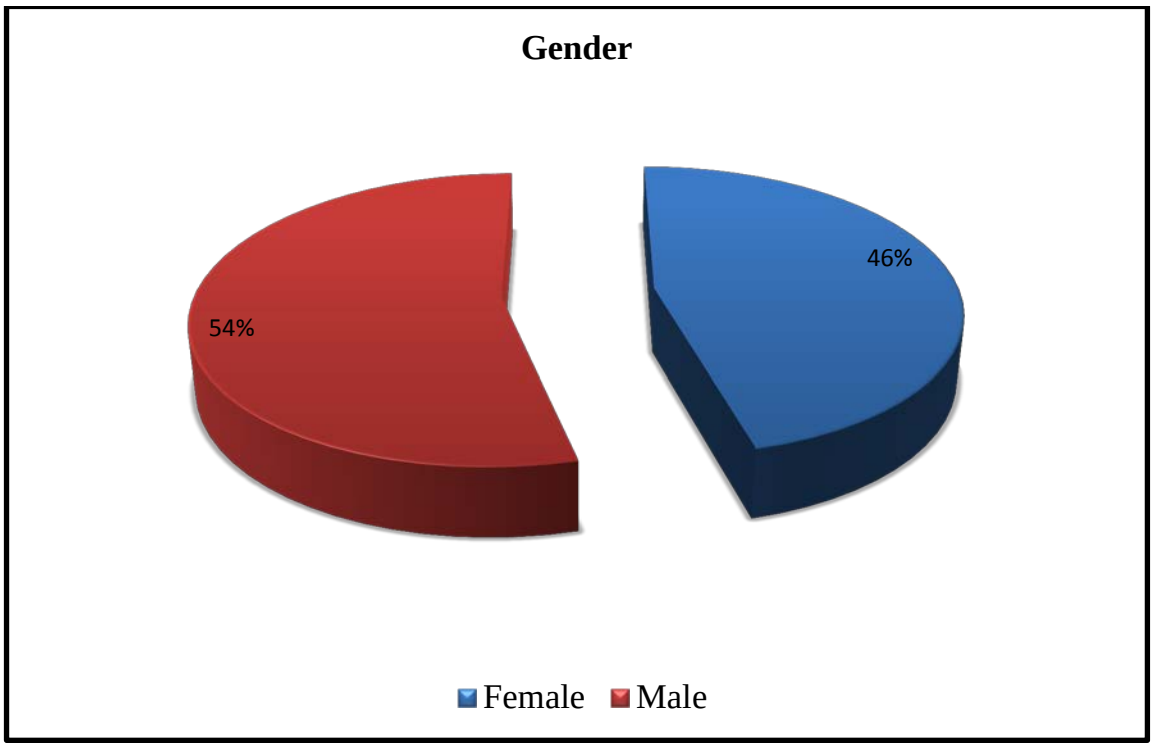
GENDER DISTRIBUTION

Among the study population , 54 patients were male and 46 patients were female. Male preponderance was observed in this study population.

Table 2 GENDER DISTRIBUTION

Sex		
	Frequency	**Percent**
Female	46	46.0
Male	54	54.0
Total	100	100.0

Diagram 2 GENDER DISTRIBUTION



DURATION

Duration of diabetes in study population range from 1 to 25 years

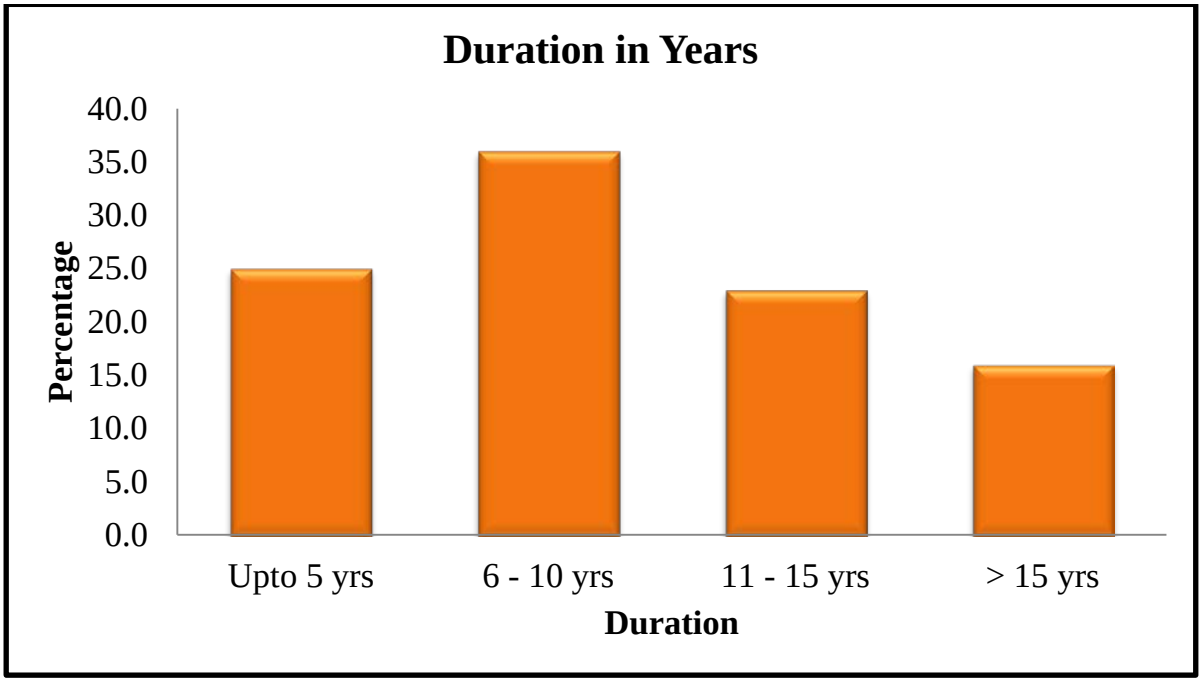
Mean duration is 10 years

In 36 percentage of study population the duration of diabetes was 6 to 10 years, in 25 persons duration was <5 years, in 23 persons it was for 11-15 years and for 16 patients it was for > 25 years.

Table 3 Frequency of diabetes with respect to duration in years

Duration		
	Frequency	**Percent**
Upto 5 yrs	25	25.0
6 - 10 yrs	36	36.0
11 - 15 yrs	23	23.0
> 15 yrs	16	16.0
Total	100	100.0

Diagram 3 Bar chart representation of duration of diabetes



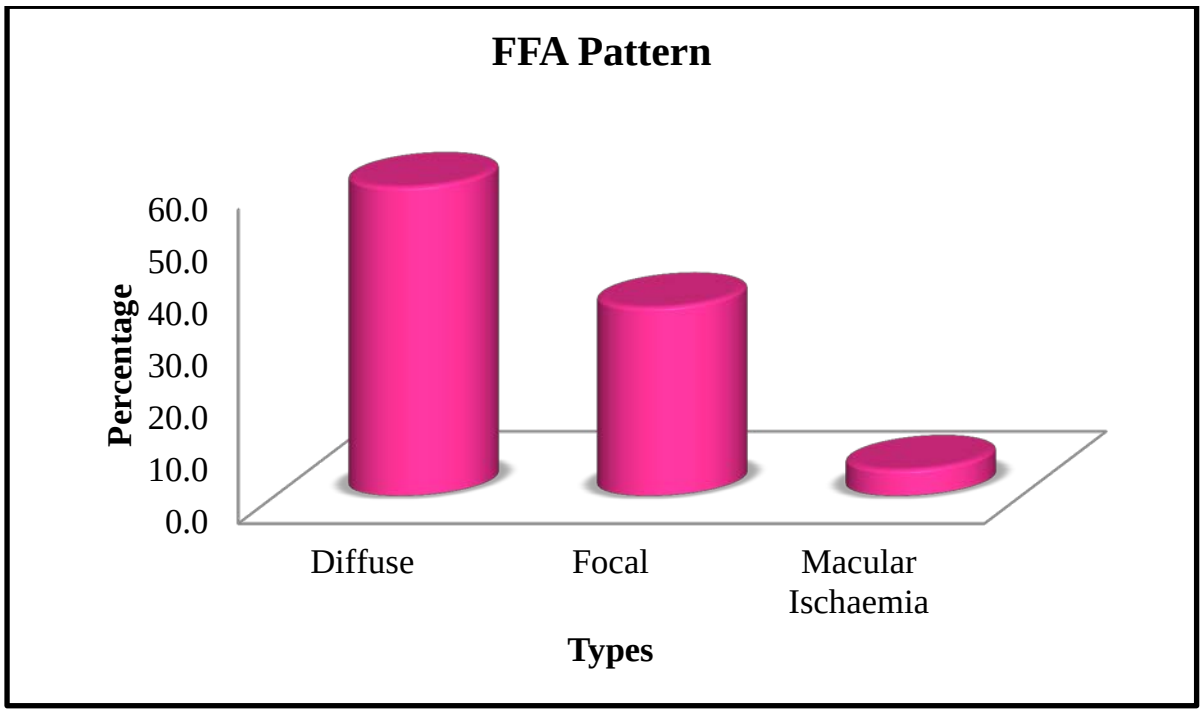
Fundus Fluorescein Angiography Pattern

CSME is classified into 3 patterns based on Fundus Fluorescein Angiography. Among the 100 patients studied diffuse maculopathy was seen in 59, focal maculopathy in 36 persons and ishchaemic type in 5 patients.

Table 4 Frequency of various types of maculopathy in fundus fluorescein angiography

FFA Pattern		
	Frequency	**Percent**
Diffuse	59	59.0
Focal	36	36.0
Macular Ischaemia	5	5.0
Total	100	100.0

Diagram 4 Bar chart representation of FFA pattern



BEST CORRECTED VISUAL ACUITY

Among the 100 patients studied, Best Corrected Visual Acuity was between 6/6 to 6/18 in 44 patients, 6/24 to 6/60 in 40 patients and 1/60 to 5/60 in 16 patients.

Table 5 Best Corrected Visual Acuity

Best Corrected Visual Acuity		
	Frequency	**Percent**
6/6 to 6/18	44	44.0
6/24 to 6/60	40	40.0
1/60 to 5/60	16	16.0
Total	100	100.0

Diagram 5 Bar chart representation of Best Corrected Visual Acuity

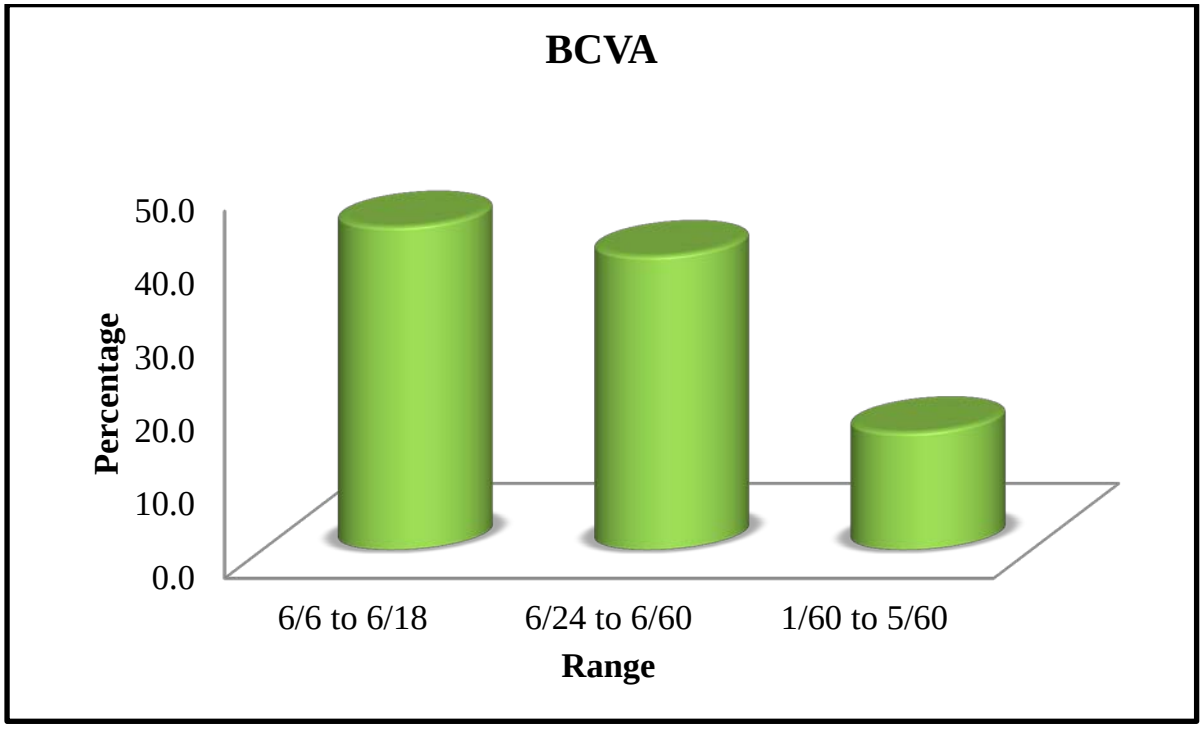


Table 6 :Physical activity

52 percent of study population had brisk physical activity by walking daily for half an hour or more and most of the patients were manual labourers in agricultural and construction works.

Physical Activity		
	Frequency	**Percent**
No.	48	48.0
Yes	52	52.0
Total	100	100.0

Table 7: Insulin treatment

42 percent of study population were on insulin treatment and the rest were on oral hypoglycemic agents

Insulin Treatment		
	Frequency	**Percent**
Insulin	42	42.0
No	58	58.0
Total	100	100.0

Table 8- Frequency table of Alcohol Intake

18 percent of study population had habit of taking alcohol with 2 patients consuming alcohol daily , 10 patients consuming once in a week and others consuming occasionally

Alcohol		
	Frequency	**Percent**
No	82	82.0
Yes	18	18.0
Total	100	100.0

Table 9 –Frequency table of smoking

18 percent of study population had habit of smoking daily ,15 patients were smoking 5- 10 cigarettes and other patients were using more than one pack per day

Smoking / Tabacco		
	Frequency	**Percent**
No	82	82.0
Yes	18	18.0
Total	100	100.0

Table 10-Frequency table diet

93 percent of study population were non-vegetarian by diet and taking weekly or twice weekly

Diet		
	Frequency	**Percent**
Non – Veg.	93	93.0
Veg.	7	7.0
Total	100	100.0

Table 11 - Abdominal circumference

Abdominal circumference was measured at the level of umbilicus in cms, for males < 90cm and for females < 90 cm is normal and 57 percent of study population had increased abdominal circumference

Abdominal Circumference		
	Frequency	**Percent**
< 90 / < 100	43	43.0
> 90 / > 100	57	57.0
Total	100	100.0

Table 12 –Frequency of Body Mass Index

68 percentage of patients had normal body mass index BMI of 19-25, 29 percent were overweight with BMI >25 , 3 percent of patients were obese BMI>30

BMI		
	Frequency	**Percent**
Normal	68	68.0
Overweight	29	29.0
Obese	3	3.0
Total	100	100.0

Table 13 - Systemic hypertension

54 percentage of patients had associated systemic hypertension and were on regular treatment

SHT		
	Frequency	**Percent**
No	46	46.0
Yes	54	54.0
Total	100	100.0

Table 14-Frequency of nephropathy

20 percentage of the patients had associated nephropathy with proteinuria and serum creatinine level being more than 1.5 mgs%

Nephropathy		
	Frequency	**Percent**
No	80	80.0
Yes	20	20.0
Total	100	100.0

Table 15 –Frequency table coronary artery disease

10 percentage of the study population had associated coronary artery disease and were on treatment

CAD – Coronary Artery Disease		
	Frequency	**Percent**
No	90	90.0
Yes	10	10.0
Total	100	100.0

Table 16 – Frequency table neuropathy

15 percentage of the study population had associated neuropathy elicited by history of numbness , pins and needle sensation in the foot

Neuropathy		
	Frequency	**Percent**
No	85	85.0
Yes	15	15.0
Total	100	100.0

Table 17 – Frequency table stroke

7 percentage of population had stroke in the past

Stroke		
	Frequency	**Percent**
No	93	93.0
Yes	7	7.0
Total	100	100.0

Table 18 – Frequency table hemoglobin

For males, normal level of haemoglobin is >13 gms %, for females normal level of haemoglobin is >12gma% 93 percentage of subjects had anaemia.

Hemoglobin		
	Frequency	**Percent**
< 12 /< 13	93	93.0
> 12 / > 13	7	7.0
Total	100	100.0

Table 19 – Frequency table of total cholesterol

36 percent of patients had borderline level of total cholesterol (200-239 mg/dl), 19 percentage of patients had increased total cholesterol (>240mg/dl)

Total Cholesterol		
	Frequency	**Percent**
Normal	45	45.0
Borderline	36	36.0
High	19	19.0
Total	100	100.0

Table 20 - Frequency table of HbA1c

73 percent of the patients had poor glycaemic control HbA1C >7.6%, 19 percent had fair control 6.9- 7.6% only 8 percent had good glycaemic control in the range of 6.3 to 6.8 %

HbA1c		
	Frequency	**Percent**
Good control	8	8.0
Fair control	19	19.0
Poor control	73	73.0
Total	100	100.0

CORRELATION OF FFA PATTERN OF CSME WITH SEVERITY OF DIABETIC RETINOPATHY

Among the 100 patients, 11 patients had mild NPDR, 38 patients had moderate NPDR, 23 patients had severe NPDR, 22 patients had PDR

Diffuse maculopathy was seen in large number of subjects, of this 5 patients had mild NPDR, 18 patients had moderate NPDR, 17 patients had severe NPDR and 19 patients had PDR amounting to a total of 59

Focal maculopathy was present in 36 patients, of which 6 patients had mild NPDR, 19 had moderate NPDR, 6 had severe PDR, 5 had PDR

4 patients with proliferative diabetic retinopathy and 1 patient with moderate NPDR had ischaemic maculopathy.

Statistical analysis with chi-square test showed significant association between severity of maculopathy and severity of diabetic retinopathy with P-value being **0.015.**

Table 21: Correlation of severity of diabetic retinopathy with FFA pattern

DR * FFA pattern Cross tabulation						
			FFA pattern			
			Diffuse	Focal	Macular Ischaemia	Total
DR	Mild NPDR	Count	5	6	0	11
		%	8.5%	16.7%	0.0%	11.0%
	Moderate NPDR	Count	18	19	1	38
		%	30.5%	52.8%	20.0%	38.0%
	Severe NPDR	Count	17	6	0	23
		%	28.8%	16.7%	0.0%	23.0%
	PDR	Count	19	5	4	28
		%	32.2%	13.9%	80.0%	28.0%
Total		Count	59	36	5	100
		%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	**df**	**Asymptotic Significance (2-sided)**
Pearson Chi-Square	15.715[a]	6	.015
Likelihood Ratio	16.172	6	.013
N of Valid Cases	100		

FFA pattern of CSME had significant association with severity of Diabetic Retinopathy with p-value being 0.015

Diagram 6: Compound bar chart showing FFA pattern of maculopathy in relation with severity of diabetic retinopathy

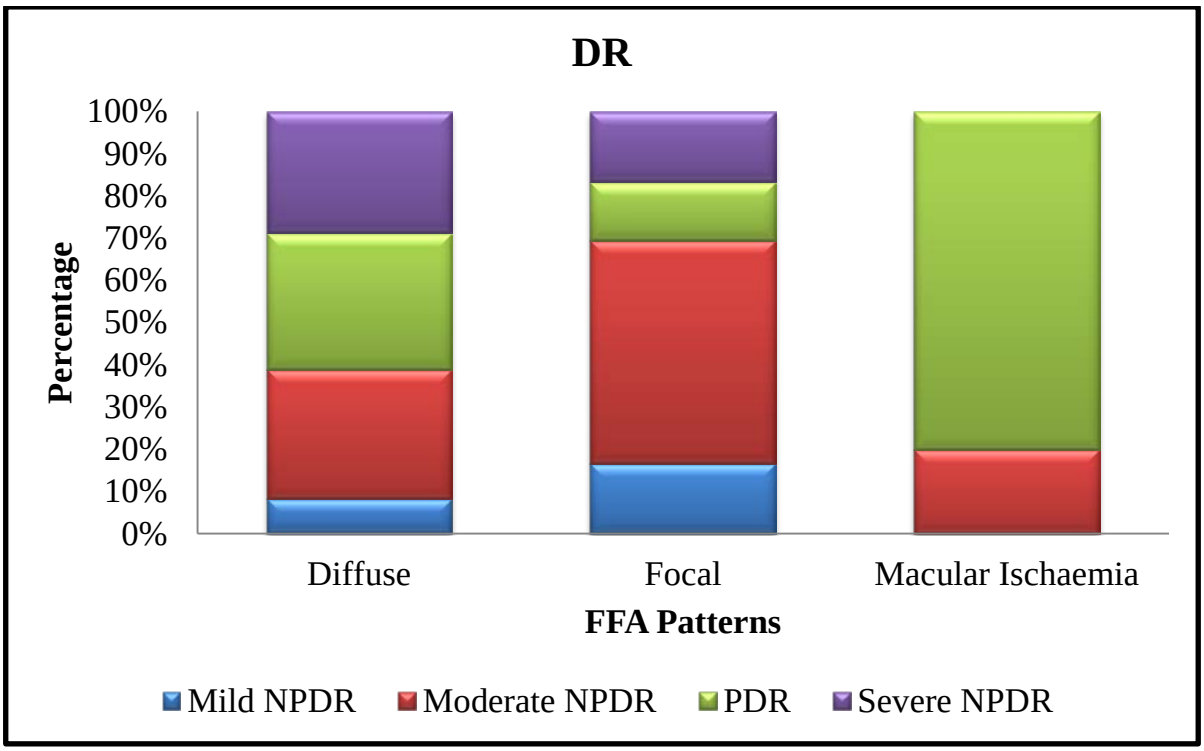
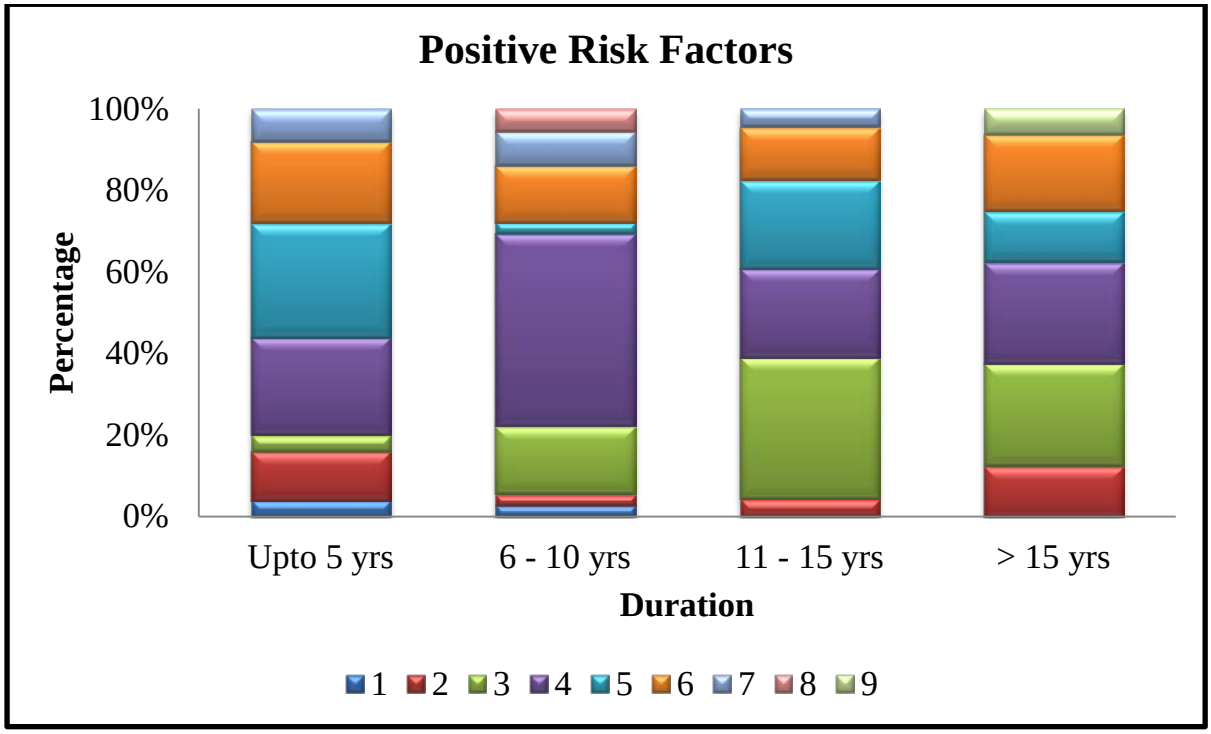


TABLE 22: Association between duration of diabetis with number of positive risk factors

Positive risk factors * duration in years Cross tabulation							
			duration in years				Total
			Upto 5 yrs	6 - 10 yrs	11 - 15 yrs	> 15 yrs	
Positive risk factors	1	Count	1	1	0	0	2
		%	4.0%	2.8%	0.0%	0.0%	2.0%
	2	Count	3	1	1	2	7
		%	12.0%	2.8%	4.3%	12.5%	7.0%
	3	Count	1	6	8	4	19
		%	4.0%	16.7%	34.8%	25.0%	19.0%
	4	Count	6	17	5	4	32
		%	24.8%	47.2%	21.7%	25.0%	32.0%
	5	Count	7	1	5	2	15
		%	28.0%	2.8%	21.7%	12.5%	15.0%
	6	Count	5	5	3	3	16
		%	20.0%	13.9%	13.0%	18.8%	16.0%
	7	Count	2	3	1	0	6
		%	8.0%	8.3%	4.3%	0.0%	6.0%
	8	Count	0	2	0	0	2
		%	0.0%	5.6%	0.0%	0.0%	2.0%
	9	Count	0	0	0	1	1
		%	0.0%	0.0%	0.0%	6.3%	1.0%
Total		Count	25	36	23	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Diagram 7 :Association between duration of diabetes mellitus with number of positive risk factors



Chi Square Tests had P value of 0.111. Even though the correlation between duration of diabetes with number positive risk factors is not statistically significant, it was noted that the patients with 4 to 6 positive risk factors developed maculopathy within 5 years of diabetes.

CORRELATION BETWEEN DURATION OF DIABETES AND SEVERITY OF DIABETIC RETINOPATHY

Among 100 patients, 25 patients had diabetes for less than 5 years, 36 patients had diabetes for 6-10 years , 23 patients had for 11 – 15 years, 16 patients were having diabetes for more than 15 years. In mild NPDR, severe NPDR, PDR group more number of patients were in 6-10 years. In moderate NPDR group more number of patients were in 6-10 years.

Chi- square tests showed no statistically significant association between duration of diabetes and severity of diabetic retinopathy.

Table 23: Correlation between duration of diabetes and severity of diabetic retinopathy

DR * duration in years Cross tabulation							
			duration in years				Total
			Upto 5 yrs	6 - 10 yrs	11 - 15 yrs	> 15 yrs	
DR	Mild NPDR	Count	0	5	3	3	11
		%	0.0%	13.9%	13.0%	18.8%	11.0%
	Moderate NPDR	Count	15	6	11	6	38
		%	60.0%	16.7%	47.8%	37.5%	38.0%
	Severe NPDR	Count	4	12	4	3	23
		%	16.0%	33.3%	17.4%	18.8%	23.0%
	PDR	Count	6	13	5	4	28
		%	24.0%	36.1%	21.7%	25.0%	28.0%
Total		Count	25	36	23	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	16.072[a]	9	.065
Likelihood Ratio	19.135	9	.024
N of Valid Cases	100		

Chi Square tests shows there is no significant association

Diagram 8

Compound bar diagram showing severity of diabetic retinopathy with respect to duration of diabetes mellitus

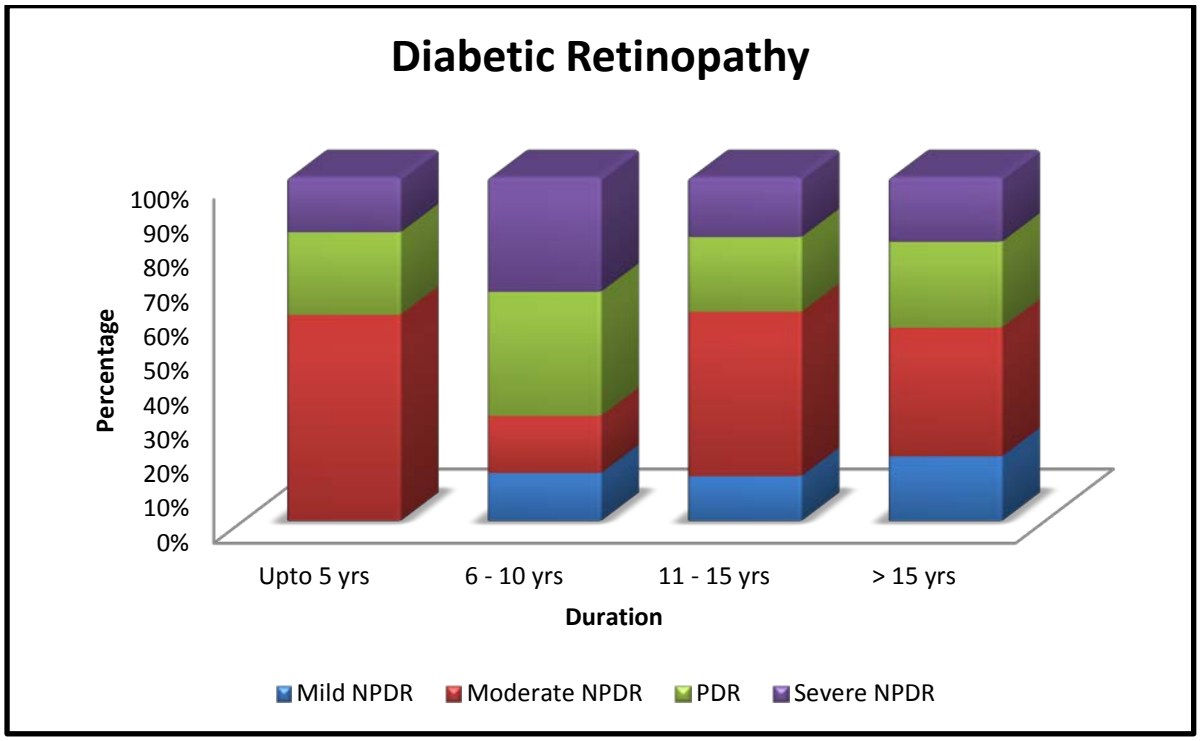


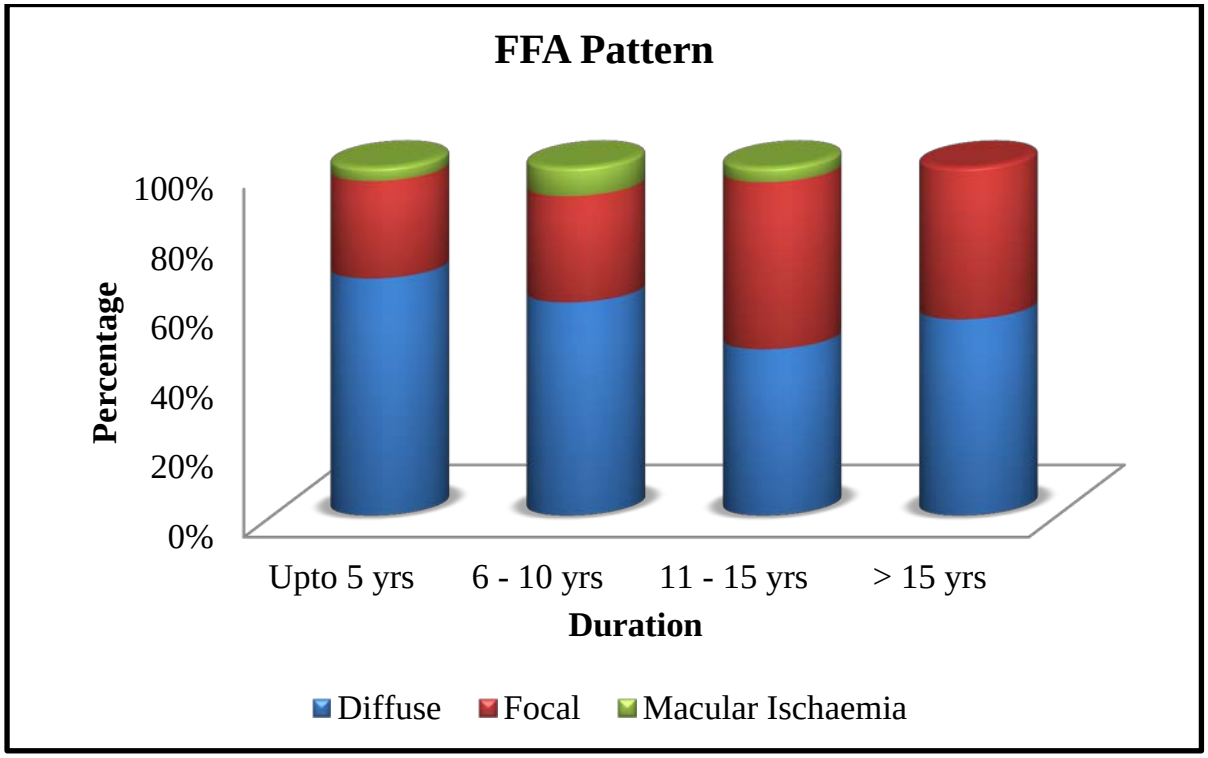
Table 24: Correlation of FFA pattern with duration of diabetes mellitus

Maximum number of patients with maculopathy had diabetes for 6-10 years. In this group 22 patients had diffuse maculopathy, 11 patients had focal maculopathy and 3 had ischaemic maculopathy. P value of chi-square test is 0.616 and it shows no statistical significance.

FFA pattern * duration in years Cross tabulation							
			duration in years				Total
			Upto 5 yrs	6 - 10 yrs	11 - 15 yrs	> 15 yrs	
FFA pattern	Diffuse	Count	17	22	11	9	59
		%	68.0%	61.1%	47.8%	56.3%	59.0%
	Focal	Count	7	11	11	7	36
		%	28.0%	30.6%	47.8%	43.8%	36.0%
	Macular ischaemia	Count	1	3	1	0	5
		%	4.0%	8.3%	4.3%	0.0%	5.0%
Total		Count	25	36	23	16	100
		%	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	4.449[a]	6	.616
Likelihood Ratio	5.088	6	.533
N of Valid Cases	100		

Diagram 9 : Correlation of FFA pattern with duration of diabetes



ASSOCIATION OF FOCAL MACULOPATHY WITH SYSTEMIC RISK FACTORS

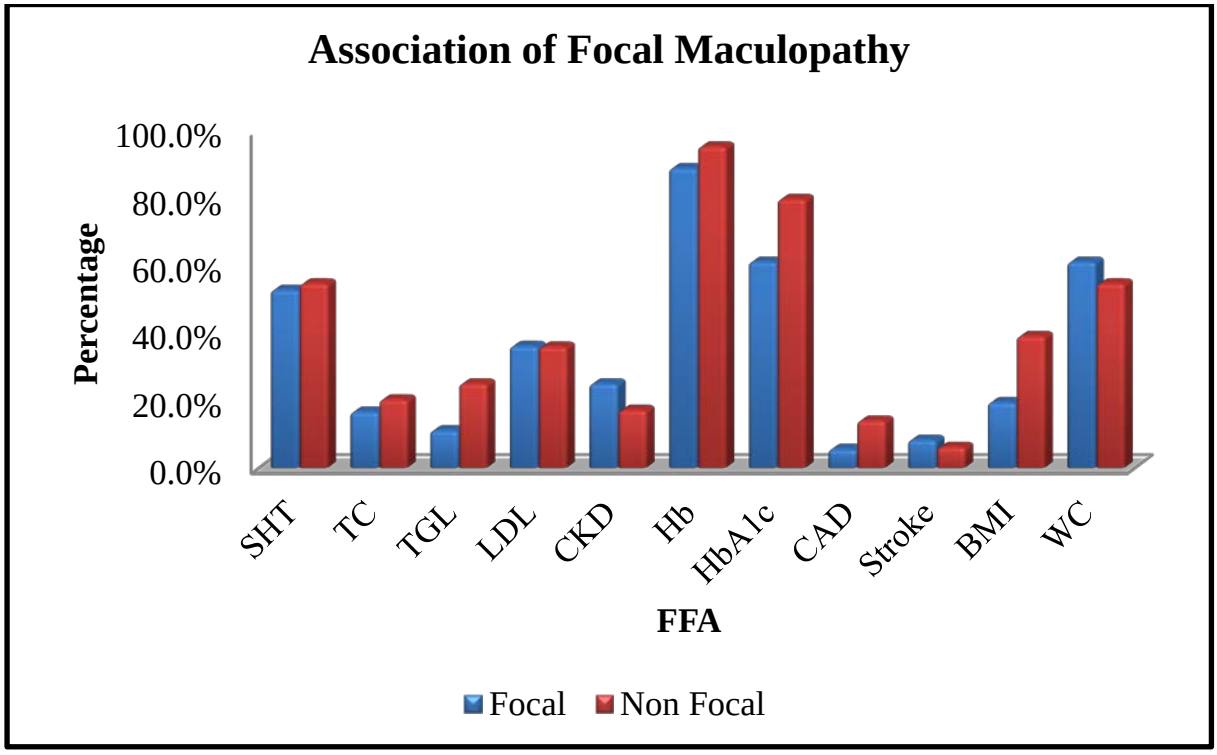
To find the association of focal maculopathy with various systemic risk factors, the 100 patients were divided into two groups as those having focal maculopathy and others. On analysing the risk factors Body mass index had statistically significant association with p-value being 0.044.

Table 25 : Association of focal maculopathy with multiple risk factors

Association of focal maculopathy with systemic risk factors						
		FFA		Total	x 2 - value	P-value
		Focal	Non Focal			
SHT	Count	19	35	54	0.034	0.854 #
	%	52.8%	54.7%	54.0%		
TC	Count	6	13	19	0.233	0.894 #
	%	16.7%	20.3%	19.0%		
TGL	Count	4	16	20	5.093	0.078 #
	%	11.1%	25.0%	20.0%		
LDL	Count	13	23	36	0.025	0.988 #
	%	36.1%	35.9%	36.0%		
Nephropathy	Count	9	11	20	0.879	349 #
	%	25.0%	17.2%	20.0%		
Hb	Count	32	61	93	1.46	0.227 #
	%	88.9%	95.3%	93.0%		
HbA1c	Count	22	51	73	5.05	0.080 #
	%	61.1%	79.7%	73.0%		
CAD	Count	2	9	10	4.899	0.086 #
	%	5.6%	14.1%	10.0%		
Stroke	Count	3	4	7	0.154	0.700 #
	%	8.3%	6.3%	7.0%		
BMI	Count	7	25	32	4.075	0.044 *
	%	19.4%	39.1%	32.0%		
WC	Count	22	35	57	0.388	0.533 #
	%	61.1%	54.7%	57.0%		
* Sig at P < 0.05 and # No Significance at P > 0.05 level						

Analysis of multiple risk factors with focal maculopathy elucidated that Body Mass Index is having statistically significant association with P value being 0.044

Diagram 10:Association of focal maculopathy with multiple risk factors.



ASSOCIATION OF DIFFUSE MACULOPATHY WITH SYSTEMIC RISK FACTORS

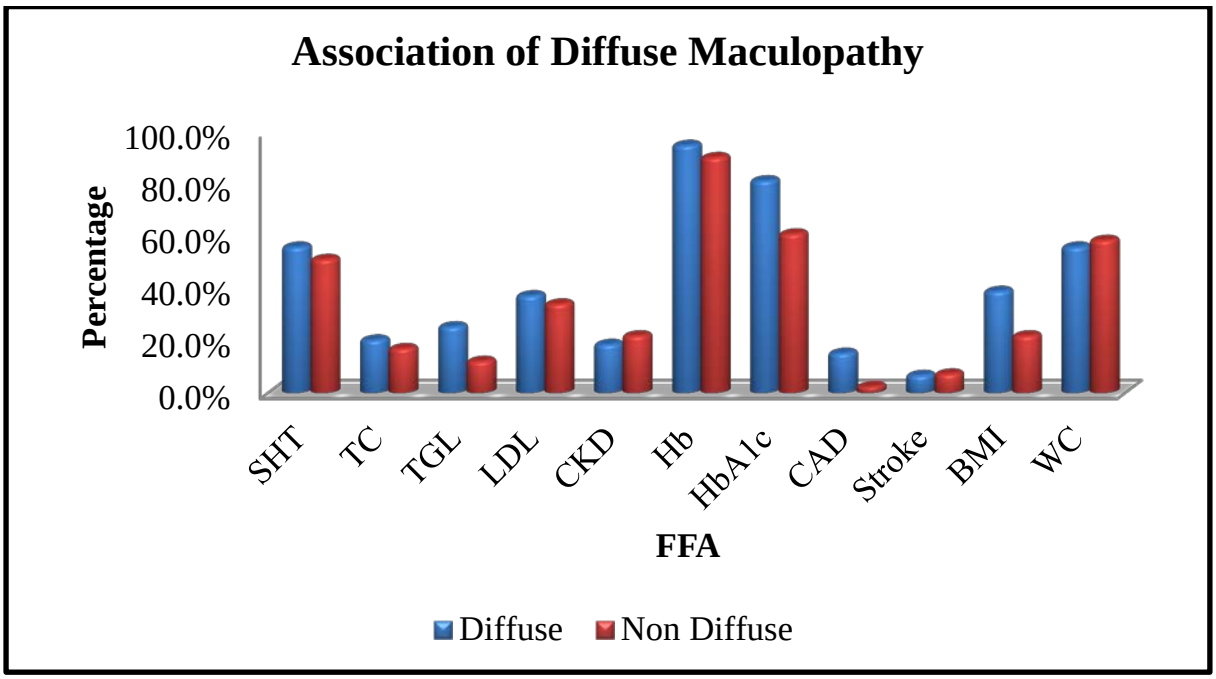
The association between diffuse maculopathy with systemic risk factors is analysed by dividing the 100 patients into two groups, one group comprises those having diffuse maculopathy and the rest of the patients in other group. Of all the risk factors analysed HbA1c is having statistically significant association with diffuse maculopathy with p value being 0.026.

Table 27: Association of diffuse maculopathy with multiple risk factors

Association of diffuse maculopathy with risk factors						
		FFA		Total	x2 - value	P-value
		Diffuse	Non Diffuse			
SHT	Count	33	21	54	0.216	0.642 #
	%	55.9%	51.2%	54.0%		
TC	Count	12	7	19	0.423	0.809 #
	%	20.3%	17.1%	19.0%		
TGL	Count	15	5	20	4.101	0.129 #
	%	25.4%	12.2%	20.0%		
LDL	Count	22	14	36	1.907	0.385 #
	%	37.3%	34.1%	36.0%		
Nephropathy	Count	11	9	20	0.165	0.684 #
	%	18.6%	22.0%	20.0%		
Hb	Count	56	37	93	0.811	0.440 #
	%	94.9%	90.2%	93.0%		
HbA1c	Count	48	25	73	7.323	0.026 *
	%	81.4%	61.0%	73.0%		
CAD	Count	9	1	10	5.704	0.058 #
	%	15.3%	2.4%	10.0%		
Stroke	Count	4	3	7	0.011	1.00 #
	%	6.8%	7.3%	7.0%		
BMI	Count	23	9	32	3.225	0.073 #
	%	39.0%	22.0%	32.0%		
WC	Count	33	24	57	0.067	0.796 #
	%	55.9%	58.5%	57.0%		
* Sig at P < 0.05 and # No Significance at P > 0.05 level						

Analysis of multiple risk factors with Diffuse maculopathy elucidated that HbA1c had statistically significant association with P value 0.026

Diagram 12:Association of diffuse maculopathy with multiple systemic risk factors



According to duration of Diabetes Mellitus study population were divided in to four groups and the various risk factors are divided in to three groups as follows

GROUP I – Patients had only physical risk factors namely BMI, AC, ALCOHOL, SMOKING, PHYSICAL INACTIVITY.

GROUP II – Patients having abnormal blood parameters namely HAEMOGLOBIN, HbA1c, SERUM CHOLESTEROL,

GROUP III – Patients having other Systemic Diseases like SHT, NEPHROPATHY, CAD, and STROKE.

1. The total number of CSME patients in group 1 were 7, in this group with only physical risk factors none (0%) were affected in < 5 years duration, 42 % (3 patients) affected in 6-10 years duration, 28 %(2 patients) affected in 11-15 years duration, and 28%(2 patients) affected in more than 15 years duration.
2. In group 2 patients with abnormal blood parameters the incidence percentage is more within 10 years duration, 29% in <5 years duration, 35% in 5-10 years duration, 16% in 11-15 years duration and 19% in >15 years duration.
3. In group 3 patients with other associated systemic risk factors, 31 % of patients affected within 5 years duration, 37 % affected in 6-10 years duration, 22% in 10-15 years duration and 15% in >15 years duration.

Table 28: Comparision of duration with grouped risk factors

Duration * Groups Cross tabulation					
		Groups			Total
		Group I	Group II	Group III	
Duration	>15 years	2(28%)	6(19%)	9(15%)	17
	11-15 years	2(28%)	5(16%)	13(22%)	20
	5-10 years	3(42%)	11(35%)	22(37%)	36
	Upto 5 years	0(0%)	11(29%)	18(31%)	27
Total		7	31	62	100

Diagram 13: Comparision of duration with grouped risk factors

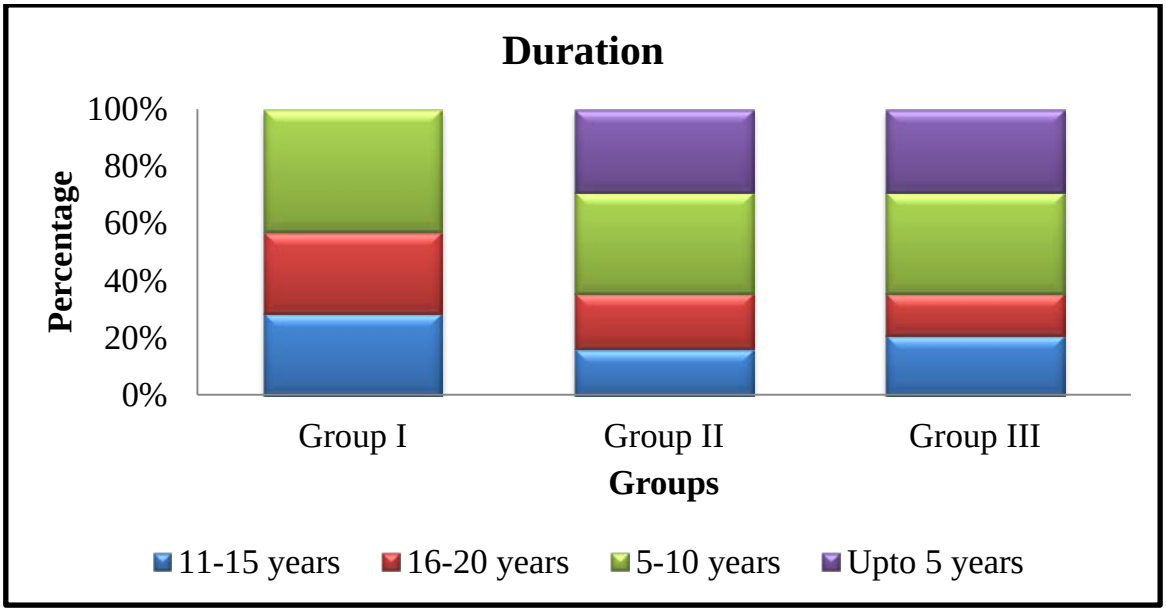


Table 28

Chi-Square Tests			
	Value	df	Asymptotic Significance (2-sided)
Pearson Chi-Square	3.526[a]	6	.740
Likelihood Ratio	5.306	6	.505
N of Valid Cases	100		

Even though the Chi Square test shows p value of 0.740 which is not clinically significant , in accordance with the risk factor, patients in group 1(with physical risk factors only) and with diabetes of less than 5 years duration did not have CSME but the other two groups with more number of risk factors, CSME occurred within 5 years.

13. SUMMARY

- The mean age group of the study population having CSME is 57 years
- Maximum frequency is in the age group of 51 to 60 years
- There is male preponderance with 54%.
- The mean duration of diabetes is 10 years
- Maximum frequency is in the duration of 6 to 10 years which is 36%
- The FFA pattern of CSME was 59% diffuse maculopathy, 36% focal maculopathy, 5% macular ischemia.
- The incidence of CSME in relation to severity of diabetic retinopathy is as follows

  Mild NPDR – 11%
  Moderate NPDR -38%
  Severe NPDR – 23%
  PDR – 28%

In this study the incidence is higher in moderate NPDR group.

- Among the study population 68% had normal body mass index, 29% were overweight and 3% were obese.
- Abdominal circumference was normal for 43% and increased for 57%.
- 93% of CSME patients were anaemic and 7% had normal haemoglobin level.
- Out of 100 patients 73% had poor glycaemic control, 19% had fair glycaemic control and 8% had good glycaemic control.
- Total cholesterol was high in 19%, 36 % borderline and 45% within normal limits.
- Proteinuria was present in 31% of patients.

14. DISCUSSION

I. Association of severity of Diabetic retinopathy with FFA pattern of CSME showed with P value 0.015

II. Analysis of multiple risk factors

1. Focal maculopathy had significant association with body mass index with P value being 0.044
2. Diffuse maculopathy had significant association with HbA1c with p-value being 0.026.

III. 5% of Patients had ischemic type of CSME, among these 5 patients 4 patients had Proliferative diabetic retinopathy and 1 patient had moderate NPDR. All the 5 patients were Anaemic, 4 patients had poor glycaemia control.

IV. According to the duration of diabetes mellitus the study population was divided into four groups and was compared for association with the risk factors after grouping the risk factors as physical risk factors, abnormal blood parameters and other systemic diseases

1. The total number of CSME patients in group 1 were 7, in this group with only physical risk factors none (0%) were affected in < 5 years duration, 42 % (3 patients) affected in 6-10 years duration, 28 %(2 patients) affected in 11-15 years duration, and 28%(2 patients) affected in more than 15 years duration.
2. In group 2 patients with abnormal blood parameters the incidence percentage is more within 10 years duration, 29% in <5 years duration, 35% in 5-10 years duration, 16% in 11-15 years duration and 19% in >15 years duration.

3. In group 3 patients with other associated systemic risk factors, 31 % of patients affected within 5 years duration, 37 % affected in 6-10 years duration, 22% in 10-15 years duration and 15% in >15 years duration.

In accordance with the risk factor, patients in group 1(with physical risk factors only) and diabetes of less than 5 years duration did not have CSME but the other two groups with more number of risk factors CSME occurred within 5 years.

15. CONCLUSION

In the analysis of systemic risk factors, a significant correlation was found to exist between abnormal BMI and focal maculopathy and diffuse maculopathy was associated with increased levels of HbA1c. Patients with more number of risk factors developed CSME within a period of 5 years, even with adequate glycaemic control

PART III

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17. PROFORMA

Name :

Age :

Gender :

IP /OP no :

Address :

Occupation :

Family income :

Chief complaints :

Past medical or

surgical history :

Personal history : Alcohol, tobacco, physical activity, diet

Age at diagnosis of type 2 DM :

Duration of Diabetes mellitus :

Age at onset of diabetes treatment :

Nature of treatment : diet or oral anti hyper glycemic drugs or insulin

Family history of Diabetes mellitus :

Systemic hypertension :

Antihypertensive medications :

Diuretic use :

Coronary artery disease :

Renal disease :

Stroke :

Nephropathy :

Neuropathy :

Clinical examination

Blood pressure measurement- Systolic BP >140 mmhg, Diastolic BP >90 mmhg;

Body Mass Index- weight (kg)/height in metre square

Underweight- <18.50

Normal- 18.50-24.99

Overweight – >25.00

Obese - >30

Note: Based on WHO criteria, BMI is age independent and the same for both sexes

Investigations:

- Blood sugar- Fasting ->126 mg/dl ,Postprandial ->200 mg/dl or Random blood sugar >200mg/dl
- ECG- evidence of previous myocardial infarction or ischemic changes (elevation/depression of S-T segment, inversion of T-wave) on ECG supported by clinical history and/or echocardiogram, or a history of cardiovascular surgery or angioplasty for IHD.
- Lipid profile-Fasting total serum cholesterol level >240mg/dl, serum triglyceride ->200mg/dl, serum LDL->190mg/dl ,serum HDL<40mg/dl.
- Nephropathy: Urine albumin>1+(30mg/dl indicating gross proteinuria) or blood urea ->40 mg/dl , serum creatinine >1.5mg/dl
- Anaemia- haemoglobin <12 gm% in females ,<13 gm% in males
- HbA1c-Normal range4.2-6.2% , Good control-6.3-6.8%, Fair control-6.9-7.6% ,Poor control >7.6%.

Eye Examination:

- Visual acuity testing with snellen chart
- Slit lamp examination
- Amsler’s grid test
- Fundus examination with a direct ophthalmoscope, indirect ophthalmoscope.
- Slit lamp biomicroscopy with +90 D lens
- Fundus Photography for keeping case records
- Fundus Fluorescein Angiography (FFA)

PATIENT CONSENT FORM

STUDY TITLE:

"A CROSS SECTIONAL STUDY TO EVALUATE THE ASSOCIATED SYSTEMIC RISK FACTORS IN TYPE 2 DIABETES MELLITUS PATIENTS WITH CLINICALLY SIGNIFICANT MACULAR EDEMA"

PARTICIPANT NAME : AGE : SEX: I.P. NO :

I confirm that I have understood the purpose of surgical/invasive procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

I have been explained about the possible complications that may occur during and after medical/ surgical procedure. I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving any reason.

I understand that investigator, regulatory authorities and the ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I hereby consent to participate in this study for various surgical/invasive procedures and their outcomes.

Time :

Date : Signature / Thumb Impression Of Patient

Place : Patient's name:

Signature of the Investigator : _____

Name of the Investigator : _____

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராய்ச்சி தலைப்பு :

மாகுலாவில் (கண் விழித்திரை) நீர் கோர்ப்பு உடைய நீரிழிவு நோயளிகளுக்கு உடல் ரீதியான ஆபத்து காரணிகள் குறித்த மதிப்பிட்டு ஆய்வு

பெயர்	:	தேதி	:
வயது	:	உள்நோயாளி எண்	:
பாலினம்	:	ஆய்வு சேர்க்கை எண்	:

இந்த ஆய்வின் நோக்கம் மற்றும் விவரங்கள் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது. இவ்ஆயிவில் இருந்து நான் எந்த நேரமும் பின்வாங்கலாம் என்பதையும் அதனால் எனக்கு எந்த பாதிப்பும் இல்லை என்பதையும் தெளிவாக புரிந்து கொண்டேன்.

முடிவுகளை அல்லது கருத்துகளை வெளியிடும் போதோ அல்லது ஆய்வின் போதோ என்னுடைய பெயரையோ அல்லது அடையாளங்களையோ வெளியிட மாட்டார்கள் என்பதையும் அறிந்து கொண்டேன்.

இந்த ஆய்வில் எவ்வித நிர்பந்தமும் இன்றி எனது சொந்த விருப்பத்தின் பேரில் நான் பங்கு பெறுகின்றேன்.

நான் சுயநினைவுடனும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் சேர்த்துக் கொள்ள சம்மதிக்கின்றேன்.

ஆராய்ச்சியாளர் ஒப்பம் **பங்கேற்பாளர் ஒப்பம் (அ)**

இடது பெருவிரல் ரேகை

18. MASTER CHART

S.No.	Age	sex	physical activity	duration in years	Nature of Treatment-Oral Hypoglycaemic agents	Insulin treatment	alcohol	smoking/tobacco	Diet	Family history	SHT	nephropathy	CAD-Coronary Artery	neuropathy	Stroke	BMI	BP	AC	FBS	PPBS	Total cholesterol	Serum triglycerides	VLDL	HDL	LDL	Hb	HbA1c	DR- SEVERIT	DR- SEVERIT	FFA-RE	FFA-LE	VA-RE	VA-LE
1	49	M	yes	5	OHA	no	yes	no	non-veg	no	yes	no	no	no	no	21.6	150/110	121	120	234	185	88	18	43	37	12.2	7.3	Moderate NPDR	Moderate NPDR	focal	diffuse	6/12	6/24
2	55	F	no	15	OHA	no	no	no	non-veg	no	no	no	no	no	no	24.1	140/90	109	275	396	257	108	22	54	73	9.2	9.9	Moderate NPDR	Moderate NPDR	diffuse	diffuse	6/18	6/18
3	65	F	no	5	OHA	no	No	no	non-veg	yes	yes	no	no	no	no	26.9	160/110	128	273	296	213	157	32	51	34	10.8	12.7	Mild NPDR	Moderate NPDR	diffuse	focal	6/24	6/36
4	52	F	no	5	OHA	no	no	no	non-veg	no	no	no	no	no	no	23.1	130/80	111	240	421	234	123	25	46	40	9.8	11.2	Moderate NPDR	Moderate NPDR	diffuse	diffuse	6/12	6/24
5	60	F	yes	6	OHA	no	no	no	non-veg	yes	yes	no	no	yes	no	24.3	160/100	123	146	245	224	132	26	42	24	9.5	10.6	Mild NPDR	Mild NPDR	focal	focal	6/9	6/9
6	55	F	yes	3	OHA	no	no	no	veg	yes	yes	no	no	no	no	22.8	150/90	116	292	388	238	173	34	62	24	8.7	10.5	Moderate NPDR	Moderate NPDR	diffuse	diffuse	6/18	6/18
7	50	F	no	13	OHA	no	no	no	non-veg	no	no	no	no	no	no	25.2	140/80	124	198	236	239	165	32	43	23	9.1	10.5	Severe NPDR	Severe NPDR	diffuse	diffuse	6/24	6/24
8	75	F	no	12	OHA	Insulin	no	no	veg	yes	yes	no	no	no	no	24	160/90	119	133	205	221	89	17	60	55	8.6	7.1	Severe NPDR	Severe NPDR	diffuse	focal	6/24	6/24
9	67	M	yes	2	OHA	no	NO	NO	non-veg	no	yes	no	no	no	no	23.6	150/90	126	156	232	227	176	35	42	149	10.2	8.5	Moderate NPDR	Moderate NPDR	focal	focal	6/9	6/9
10	55	M	yes	7	OHA	insulin	NO	no	non-veg	yes	yes	no	no	no	no	23.5	180/60	109	225	278	231	167	37	43	122	13.6	10.4	Severe NPDR	Severe NPDR	focal	focal	6/12p	6/12p
11	63	M	yes	11	OHA	Insulin	yes	no	non-veg	no	yes	yes	yes	no	no	22.7	170/90	126	118	214	238	158	35	38	121	11.7	9.8	Moderate NPDR	Moderate NPDR	diffuse	diffuse	RE-6/18	LE-6/18
12	58	F	yes	25	OHA	insulin	no	no	non-veg	yes	no	no	no	no	no	21.2	130/80	87	365	564	154	142	28	71	55	9.8	7.8	PDR	PDR	focal	focal	6/9	6/12
13	50	F	yes	10	OHA	insulin	no	no	non-veg	yes	yes	no	nil	yes	nil	24.8	130/80	105	90	107	217	161	32	38	147	12.5	9.6	Mild NPDR	Mild NPDR	focal	diffuse	6/12	6/18
14	54	M	yes	25	OHA	no	no	no	non-veg	no	yes	yes	no	no	no	19.4	150/90	91	195	245	231	167	37	54	138	9.5	7.8	Mild NPDR	Mild NPDR	diffuse	diffuse	RE-6/60	LE-6/60
15	53	F	yes	1	OHA	no	no	no	non-veg	no	yes	no	no	no	no	30.7	140/90	110	104	304	214	275	55	37	122	10.1	7.8	Moderate NPDR	Moderate NPDR	diffuse	diffuse	RE-6/36	LE-2/60
16	52	F	yes	10	OHA	insulin	no	no	non-veg	yes	no	no	yes	no	no	21.9	140/90	86	158	208	235	265	53	38	144	9	7.2	Mild NPDR	Mild NPDR	diffuse	diffuse	RE-6/18	LE-6/12
17	46	M	yes	5	OHA	insulin	no	yes	non-veg	yes	no	no	no	no	no	18.5	100/70	79	150	316	202	234	46	34	122	10.2	8.1	PDR	PDR	lar ischa	lar ischa	RE-2/60	LE-6/60
18	57	M	no	10	OHA	insulin	yes	yes	non-veg	yes	yes	no	yes	no	no	23.5	150/80	92	310	352	121	292	58	33	30	12.2	8.63	Moderate NPDR	Moderate NPDR	diffuse	diffuse	RE-4/60	LE-6/18p
19	65	F	yes	2	OHA	no	no	no	non-veg	no	yes	no	no	no	no	21.4	120/80	95	110	215	171	210	45	38	88	8.8	8	Severe NPDR	Severe NPDR	diffuse	diffuse	RE-1/60	LE-1/60
20	64	F	no	15	OHA	no	no	no	veg	yes	yes	no	yes	yes	no	27.6	160/100	97	106	182	138	156	31	53	72	9.4	7.1	Mild NPDR	Mild NPDR	diffuse	focal	RE-3/60	LE-6/36
21	53	M	yes	10	OHA	Insulin	no	no	non-veg	yes	SHT	yes	no	no	no	19.3	150/90	79	209	260	147	118	23	41	82	7.1	9.2	PDR	PDR	diffuse	diffuse	RE-6/12	LE-6/12
22	42	F	yes	6	OHA	insulin	no	no	non-veg	yes	no	no	no	no	no	21.5	150/90	75	128	320	224	160	32	7	135	7.4	6	Severe NPDR	PDR	diffuse	diffuse	RE-6/24	LE-6/18p
23	60	F	yes	1	OHA	no	no	no	non-veg	no	no	no	no	no	no	25.6	150/90	94	121	272	240	173	34	57	148	11.5	7.5	Moderate NPDR	Moderate NPDR	focal	focal	RE-6/24	LE-2/60
24	68	F	yes	15	OHA	insulin	no	no	non-veg	yes	yes	no	no	no	no	27.9	150/90	102	72	208	193	160	32	58	135	10.9	12.8	Moderate NPDR	Moderte NPDR	diffuse	diffuse	RE_6/36	LE-6/12p
25	65	F	yes	10	OHA	no	no	no	non-veg	no	yes	no	no	no	no	22.8	150/90	78	107	189	133	161	32	39	62	12.8	7.7	Mild NPDR	Moderate NPDR	diffuse	diffuse	RE-6/60	LE-6/60
26	50/F	F	no	6	OHA	no	no	no	non-veg	no	yes	no	no	no	no	21.3	140/80	84	322	391	210	171	34	50	139	12.6	11.4	PDR	PDR	diffuse	diffuse	RE-6/60	LE-6/60
27	59	M	no	15	OHA	insulin	no	no	non-veg	no	no	no	no	no	no	23.6	130/80	94	112	145	174	204	40	40	94	12	9.1	Moderate NPDR	Moderate NPDR	diffuse	focal	RE-6/12	LE-6/12
28	55	M	yes	2	OHA	no	no	no	non-veg	no	yes	no	no	no	no	24.2	150/90	93	137	236	206	224	45	34	127	8.8	7.1	Severe NPDR	PDR	diffuse	diffuse	RE-6/24p	LE-6/60
29	53	M	yes	10	OHA	no	yes	yes	non-veg	yes	yes	no	no	no	no	25.6	190/110	103	417	513	237	220	44	30	163	9.9	12	PDR	PDR	focal	diffuse	RE-6/24	LE-6/24
30	68	M	no	3	OHA	no	no	no	non-veg	no	SHT	yes	no	no	no	21.6	160/100	92	223	362	207	172	34	30	143	6.9	8.4	Mild NPDR	Moderate NPDR	focal	focal	RE-6/12	LE-6/24
31	50	F	yes	16	OHA	no	no	no	non-veg	yes	no	no	no	no	no	24.4	120/80	82	127	301	155	132	26	47	82	8.1	10.4	Severe NPDR	Moderate NPDR	diffuse	diffuse	RE-3/60	LE-6/18p
32	56	F	no	6	OHA	insulin	yes	yes	non-veg	yes	yes	no	yes	no	yes	30.5	140/70	96	181	258	198	186	37	31	130	10.4	10.9	Severe NPDR	Severe NPDR	diffuse	diffuse	RE-6/60	LE-6/24
33	59	M	yes	10	OHA	Insulin	no	no	non-veg	yes	no	no	no	no	no	25.3	130/70	79	267	420	251	228	45	59	147	10.3	14.8	Severe NPDR	Severe NPDR	diffuse	diffuse	3/60	4/60
34	73	M	yes	2	OHA	no	no	no	non-veg	no	no	no	no	no	yes	24.6	130/80	94	382	415	208	325	65	50	93	13.4	10.2	Moderate NPDR	Moderate NPDR	diffuse	focal	RE-6/18	LE-6/12
35	55	F	no	7	OHA	no	no	no	non-veg	yes	yes	no	no	no	no	24.6	160/90	91	138	124	265	204	53	61	151	11.6	11	Moderate NPDR	Moderate NPDR	focal	focal	RE-6/12	LE-6/12
36	62	F	no	7	OHA	Insulin	no	no	non-veg	yes	no	yes	no	no	no	26.1	110/70	95	256	299	209	134	26	48	135	9.1	8.2	Severe NPDR	Severe NPDR	focal	focal	RE-6/18	LE-6/18
37	62	M	yes	20	OHA	no	no	no	non-veg	yes	yes	no	yes	no	no	27	170/90	110	206	294	134	642	NA	24	NA	9.2	8.76	Severe NPDR	Severe NPDR	diffuse	diffuse	RE-6/12	LE-6/36
38	67	M	yes	2	OHA	no	no	no	non-veg	yes	no	no	no	no	no	23.3	130/90	95	198	439	192	251	50	40	102	10.5	9.7	PDR	PDR	diffuse	diffuse	RE-3/60	LE-1/60
39	60	M	no	10	OHA	no	no	no	veg	no	yes	no	no	no	no	23	110/70	88	88	150	158	182	36	42	80	8.2	9	Severe NPDR	Severe NPDR	diffuse	focal	RE-2/60	LE=6/24
40	59	M	no	7	OHA	no	yes	no	non-veg	yes	no	no	no	no	no	24.2	130/100	90	199	356	160	175	35	45	80	10.2	6.7	PDR	PDR	diffuse	diffuse	RE-6/12	LE-6/24
41	50	F	yes	7	OHA	no	yes	yes	non-veg	yes	no	no	no	no	no	21	140/70	78	468	513	178	169	33	32	113	9	11.2	Moderate NPDR	Moderate NPDR	focal	focal	RE-6/12	LE-6/12
42	74	F	no	14	OHA	no	no	no	veg	yes	yes	no	no	no	no	22.6	150/100	82	234	512	186	193	39	46	101	9.6	9.8	PDR	PDR	lar ischa	diffuse	RE-3/60	LE-6/60
43	58	M	yes	10	OHA	no	no	yes	non-veg	yes	yes	no	no	no	no	24.4	160/100	92	213	398	210	185	37	29	144	8.6	9	PDR	PDR	diffuse	diffuse	RE-6/18	LE-6/18
44	56	M	yes	5	OHA	no	no	yes	non-veg	yes	yes	yes	no	no	no	22	150/90	106	312	536	220	195	39	46	135	10.2	14.4	Severe NPDR	Severe NPDR	focal	diffuse	6/24	6/24
45	57	M	yes	10	OHA	no	no	no	non-veg	no	no	no	no	no	no	24	120/80	97	165	326	180	170	34	46	100	11.4	9	PDR	PDR	diffuse	diffuse	6/24	6/24
46	52	M	no	6	OHA	no	yes	no	non-veg	no	yes	yes	yes	no	no	26.6	160/100	115	210	320	170	250	50	38	88	10.2	11.4	PDR	PDR	diffuse	diffuse	6/12	6/12
47	62	F	yes	12	OHA	no	no	no	non-veg	yes	no	no	no	no	no	22	130/70	88	175	310	190	110	22	52	116	8	7.7	PDR	PDR	focal	diffuse	6/12	6/12
48	57	M	no	5	OHA	no	no	no	non-veg	yes	yes	yes	yes	yes	no	24	170/90	99	184	220	264	140	28	46	190	9	10.4	Moderate NPDR	Mild NPDR	diffuse	focal	6/12	6/12
49	53	F	yes	10	OHA	no	no	no	non-veg	yes	no	no	no	no	no	26	110/70	103	290	441	179	250	50	53	76	9	8.7	PDR	PDR	diffuse	diffuse	6/60	6/60
50	70	M	no	2	OHA	no	yes	yes	non-veg	yes	yes	yes	no	yes	yes	24	140/90	89	109	120	243	119	24	63	156	10.4	8.4	Moderate NPDR	Moderate NPDR	focal	focal	6/18	6/18
51	69	F	yes	16	OHA	insulin	no	no	non-veg	yes	no	no	no	no	no	29	140/90	100	168	176	203	133	26	57	120	8.6	8.5	Moderate NPDR	Severe NPDR	diffuse	diffuse	6/36	6/60
52	60	M	yes	10	OHA	no	yes	no	non-veg	no	no	no	no	yes	no	23.4	140/90	90	113	176	184	145	29	48	107	9.8	9	Severe NPDR	Severe NPDR	diffuse	diffuse	6/60	6/60

S.No.	Age	sex	physical activity	duration in years	Nature of Treatment-Oral Hypoglycaemic agents	Insulin treatment	alcohol	smoking/tobacco	Diet	Family history	SHT	nephropathy	CAD-Coronary Artery	neuropathy	Stroke	BMI	BP	AC	FBS	PPBS	Total cholesterol	Serum triglycerides	VLDL	HDL	LDL	Hb	HbA1c	DR- SEVERITY	DR- SEVERITY	FFA-RE	FFA-LE	VA-RE	VA-LE
53	49	F	yes	9	OHA	no	no	no	non-veg	yes	no	no	no	no	no	19	150/90	88	200	286	245	225	45	46	154	11	7.6	Moderate NPDR	Moderate NPDR	focal	o leakag	6/12	6/6
54	52	M	no	10	OHA	insulin	yes	yes	non-veg	yes	yes	yes	no	yes	no	24.1	140/90	96	174	341	168	136	27	34	107	12	10.2	Moderate NPDR	Moderate NPDR	focal	focal	6/6	6/6
55	70	F	yes	6	OHA	no	no	no	non-veg	no	no	no	no	no	no	28.9	130/80	98	201	292	196	190	38	49	109	9	7.6	Moderate NPDR	Moderate NPDR	diffuse	ular ischa	3/60	2/60
56	49	M	no	6	OHA	INsulin	yes	yes	non-veg	yes	yes	no	no	no	no	23	150/90	89	210	290	230	190	38	35	157	11.5	6.5	Severe NPDR	Severe NPDR	diffuse	diffuse	6/36	6/24
57	64	M	no	16	OHA	insulin	no	yes	non-veg	yes	yes	no	no	yes	no	28	180/100	110	225	400	280	240	48	36	196	12.2	11	Moderate NPDR	Severe NPDR	diffuse	diffuse	3/60	2/60
58	58	F	yes	17	OHA	no	no	no	non-veg	yes	yes	yes	no	no	no	25.2	160/90	102	310	450	268	210	42	38	188	9.5	12	PDR	PDR	diffuse	diffuse	4/60	3/60
59	62	F	no	18	OHA	insulin	no	no	non-veg	yes	yes	yes	no	no	no	23.5	170/90	94	180	250	198	170	34	59	105	8	8.4	Severe NPDR	Severe NPDR	focal	diffuse	6/18	6/24
60	56	F	yes	10	OHA	no	yes	no	non-veg	yes	yes	no	no	no	no	26	150/80	108	245	400	220	185	37	65	118	8	10	Severe NPDR	Severe NPDR	diffuse	diffuse	2/60	4/60
61	52	M	no	14	OHA		yes	no	non-veg	no	yes	no	no	no	no	23.7	140/80	96	180	324	205	182	36	69	162	9	8.4	PDR	PDR	diffuse	focal	6/36	6/24
62	62	M	no	15	OHA	no	no	yes	non-veg	no	yes	yes	yes	no	no	26	150/90	112	216	350	245	190	38	55	152	10	9	PDR	PDR	diffuse	focal	6/60	6/18
63	44	F	yes	4	OHA	no	no	no	non-veg	no	no	no	no	no	no	21.2	140/80	86	157	342	210	175	35	47	128	7.5	9	Severe NPDR	Severe NPDR	focal	diffuse	6/18	6/12
64	41	F	yes	5	OHA	no	no	no	non-veg	yes	no	no	no	no	no	23.4	140/100	96	190	240	190	180	36	58	96	8	9	PDR	PDR	diffuse	diffuse	6/36	6/36
65	54	M	yes	8	OHA	insulin	yes	no	non-veg	yes	yes	yes	no	no	yes	25.3	160/90	115	240	367	240	214	42	31	141	10	10.7	Severe NPDR	Severe NPDR	diffuse	diffuse	6/24	6/36
66	60	F	no	20	OHA	insulin	no	no	non-veg	no	no	no	no	no	no	27	150/80	110	190	240	180	150	30	68	82	9	7	PDR	PDR	diffuse	diffuse	6/24	6/24
67	42	M	yes	7	OHA	insulin	no	yes	non-veg	yes	yes	yes	no	no	no	25	190/100	98	218	450	260	190	38	40	182	8.8	11.4	PDR	PDR	diffuse	diffuse	6/24	6/18
68	50	M	yes	10	OHA	insulin	no	no	non-veg	yes	yes	no	no	no	no	24	130/80	108	240	371	192	165	33	57	102	12	10	PDR	PDR	diffuse	diffuse	5/60	6/60
69	65	M	no	20	OHA	insulin	no	no	non-veg	yes	no	no	no	no	no	28	140/70	110	178	230	178	160	32	48	98	10	10.2	Moderate NPDR	Moderate NPDR	focal	focal	6/9	6/18
70	55	M	yes	10	OHA	no	no	no	non-veg	yes	no	no	no	no	yes	26	160/90	101	150	200	211	175	35	47	129	8	7	Moderate NPDR	Moderate NPDR	diffuse	diffuse	6/18	6/24
71	58	F	no	13	OHA	INsulin	no	no	non-veg	yes	yes	no	no	yes	no	25	170/90	97	124	250	260	170	34	47	169	9	7.8	Moderae NPDR	Mild NPDR	diffuse	focal	6/18	6/18
72	62	F	no	16	OHA	insulin	no	no	non-veg	no	no	no	no	no	no	23	130/70	102	150	200	190	145	29	49	112	12	6.4	Mild NPDR	Mild NPDR	focal	focal	6/12	6/12
73	42	M	yes	7	OHA	no	yes	yes	non-veg	yes	yes	no	no	no	no	22.1	180/100	92	154	270	240	150	30	54	156	8.2	8	PDR	PDR	lar ischa	diffuse	6/60	5/60
74	52	M	yes	10	OHA	no	no	no	non-veg	yes	no	yes	no	no	no	28	150/80	114	176	240	236	170	34	36	176	10	8	PDR	PDR	diffuse	diffuse	6/24	6/36
75	45	F	no	5	OHA	no	no	no	non-veg	yes	yes	no	no	no	no	22	160/90	87	190	270	204	130	26	45	133	8	7.4	Moderate NPDR	Moderate NPDR	focal	focal	6/9	6/12
76	55	F	no	12	OHA	no	no	no	veg	yes	no	no	no	no	no	22.1	150/90	101	214	412	190	145	29	65	96	9	8.1	Severe NPDR	Severe NPDR	diffuse	focal	6/24	6/12
77	62	M	yes	7	OHA	no	no	no	non-veg	no	no	no	no	no	yes	21.1	120/80	97	210	314	200	140	28	65	107	10.2	8.1	Severe NPDR	Severe NPDR	diffuse	focal	6/18	6/9
78	55	M	yes	15	OHA	insulin	no	no	non-veg	no	no	no	no	no	no	23	120/70	107	150	211	180	130	26	58	96	10.8	6.9	Moderate NPDR	Moderate NPDR	focal	focal	6/12	6/12
79	67	M	no	17	OHA	INSULIN	no	no	non-veg	yes	yes	no	no	no	no	23.4	160/90	98	119	240	190	130	26	60	104	10	7.1	Mild NPDR	Mild NPDR	focal	diffuse	6/12	6/18
80	50	F	no	10	OHA	insulin	no	no	non-veg	yes	no	no	no	no	no	24.2	150/90	104	245	316	175	145	29	60	86	9	8.4	PDR	PDR	diffuse	diffuse	6/60	6/60
81	61	M	no	15	OHA	Insulin	no	no	non-veg	no	no	no	no	no	no	23.4	110/70	110	124	200	180	170	34	65	71	10.6	6.5	Mild NPDR	Mild NPDR	focal	focal	6/12	6/9
82	63	M	yes	15	OHA	no	no	no	non-veg	yes	no	yes	no	no	no	20.5	110/70	114	214	360	210	160	32	65	113	11	10	Severe NPDR	Severe NPDR	focal	focal	6/24	6/18
83	60	M	no	11	OHA	no	no	no	non-veg	no	no	no	no	no	no	21.1	120/80	94	400	512	190	150	42	65	83	8.4	11.6	PDR	PDR	diffuse	diffuse	5/60	6/60
84	63	F	no	20	OHA	insulin	no	no	non-veg	yes	no	no	no	yes	no	25	170/90	104	243	367	175	160	32	67	76	11	7	PDR	PDR	diffuse	focal	6/24	6/18
85	70	M	no	18	OHA	no	no	no	non-veg	yes	yes	no	no	no	no	20.1	150/80	102	98	175	175	130	26	68	81	10.5	6.5	Mild NPDR	Moderate NPDR	focal	focal	6/24	6/18
86	53	M	yes	8	OHA	no	no	no	non-veg	yes	no	yes	no	no	no	22	140/70	96	170	400	260	170	34	38	188	10.4	9	Mild NPDR	Mild NPDR	focal	diffuse	6/18	6/18
87	65	F	yes	15	OHA	no	no	no	veg	no	no	no	no	no	no	19	110/70	105	114	184	187	154	29	67	91	7.5	7.3	Mild NPDR	Moderate NPDR	focal	focal	6/12	6/18
88	62	M	no	15	OHA	insulin	no	no	non-veg	yes	yes	no	no	yes	no	26	170/80	110	140	200	216	185	37	60	120	8.4	9	Moderate NPDR	Moderate NPDR	diffuse	focal	6/18	6/18
89	40	F	yes	6	OHA	no	no	no	non-veg	yes	yes	no	no	no	no	21.6	150/80	97	200	316	193	126	25	74	94	7.8	8.4	Severe NPDR	Moderate NPDR	diffuse	focal	6/24	6/18
90	60	M	no	20	OHA	insulin	no	no	non-veg	no	no	no	no	no	no	26	130/90	104	100	216	182	124	24	69	89	12	6.5	Moderate NPDR	Moderate NPDR	diffuse	focal	6/18	6/9
91	60	M	no	17	OHA	insulin	no	no	non-veg	no	no	no	no	no	no	25	130/80	98	126	212	170	146	29	70	71	11	7.3	Moderate NPDR	Moderate NPDR	focal	focal	6/12	6/18
92	65	F	no	14	OHA	insulin	no	no	non-veg	yes	yes	no	no	yes	yes	21.5	140/90	87	143	182	186	125	25	67	94	7.4	9	Moderate NPDR	Moderate NPDR	focal	focal	6/24	6/24
93	63	M	NO	15	OHA	insulin	yes	yes	non-veg	yes	yes	no	yes	no	no	30	160/80	110	240	312	216	160	32	76	108	11	9.4	Moderate NPDR	Moderate NPDR	diffuse	diffuse	6/60	4/60
94	55	M	yes	12	OHA	insulin	no	no	non-veg	no	yes	no	no	no	no	24.1	170/90	96	125	278	243	143	28	72	143	11.3	6.5	Mild NPDR	Moderate NPDR	diffuse	diffuse	5/60	6/60
95	49	M	yes	5	OHA	no	no	no	non-veg	yes	no	no	no	yes	no	23	130/70	107	140	200	230	256	51	66	113	12.3	9.1	Moderate NPDR	Moderate NPDR	diffuse	diffuse	6/24	6/18
96	55	F	yes	8	OHA	no	no	no	non-veg	yes	no	no	no	no	no	25.4	110/70	95	170	210	198	142	28	60	110	7	7.4	PDR	PDR	lar ischa	ular ischa	6/60	4/60
97	64	F	no	15	OHA	insulin	no	no	non-veg	yes	yes	yes	no	no	no	20.4	140/90	94	108	216	170	122	70	24	70	9	6.5	Moderate NPDR	Moderate NPDR	focal	diffuse	6/9	6/12
98	50	M	no	5	OHA	Insulin	yes	yes	non-veg	yes	yes	yes	no	no	no	20.4	130/90	93	115	236	250	186	38	34	179	8.8	8.7	Severe NPDR	Severe NPDR	diffuse	diffuse	6/24	6/18
99	53	M	no	10	OHA	insulin	no	yes	non-veg	no	no	no	no	yes	no	24	120/80	95	190	328	243	130	27	48	166	10.2	9	Severe NPDR	Severe NPDR	diffuse	diffuse	6/36	6/36
100	42	F	yes	5	OHA	no	no	no	non-veg	yes	no	no	no	no	no	24.6	110/70	89	213	310	168	126	25	74	69	8.8	7.8	Moderate NPDR	Moderate NPDR	diffuse	diffuse	6/24	6/24

19. KEY TO MASTER CHART

SHT	–	Systemic Hypertension
CAD	–	Coronary Artery Disease
BMI	–	Body Mass Index
AC	–	Abdominal Circumference
VLDL	–	Very low density lipoprotein
HDL	–	High density lipoprotein
LDL	–	Low density lipoprotein
HBA1c	–	Glycated Haemoglobin
FFA	–	Fundus Fluorescein Angiography
NPDR	–	Non Proliferative Diabetic Retinopathy
PDR	–	Proliferative Diabetic Retinopathy
CSME	–	Clinically Significant Macular Oedema