Dissertation on

THE ROLE OF FUNDUS FLUORESCEIN ANGIOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY IN DIABETIC MACULOPATHY – A CLINICAL STUDY

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CERTIFICATE

This is to certify that this dissertation entitled **"THE ROLE OF FUNDUS FLUORESCEIN ANGIOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY IN DIABETIC MACULOPATHY – A CLINICAL STUDY"** is a bonafide record of the research work done by **Dr.N.SUGANYA.,** Post graduate in Regional Institute of Ophthalmology, Madras Medical College and Research Institute, Government General Hospital,Chennai-03, in partial fulfillment of the regulations laid down by The TamilNadu Dr.M.G.R. Medical University for the award of M.S. Ophthalmology Branch III, under my guidance and supervision during the academic years 2009-2012.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"THE ROLE OF FUNDUS FLUORESCEIN ANGIOGRAPHY AND OPTICAL COHERENCE TOMOGRAPHY IN DIABETIC MACULOPATHY – A CLINICAL STUDY"** is a bonafide and genuine research work carried out by me under the guidance of Prof. Dr. Jayasungathi, M.S.D.O., Prof. Dr.Sulaiman, M.S.,D.O., Prof. Dr.Revathi M.S.,D.O., Professors, Department of Retina Services, Regional Institute of Ophthalmology & Government Ophthalmic hospital, Chennai – 600008.

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CONTENTS

PART ONE

ABBREVIATIONS

DR	-	Diabetic retinopathy
NPDR	-	Non proliferative diabetic retinopathy
PDR	-	Proliferative diabetic retinopathy
FFA	-	Fundus Fluorescein Angiography
OCT	-	Optical Coherence Tomography
WESDR	-	The Wisconsin Epidemiologic Study of Diabetic Retinopathy
DCCT	-	The Diabetes Control and Complication Trial
CSME	-	Clinically significant macular edema
ETDRS	-	The Early Treatment Diabetic Retinopathy Study
VEGF	-	Vascular endothelial growth factor

INTRODUCTION

Diabetic retinopathy (DR) is a microvascular complication of both type I and type II diabetes mellitus (DM) has become one of the leading causes of blindness world wide (Wilkinson 1988)[1]. It is a preventable blindness. DR is due to microangiopathy affecting the pre capillary arterioles, capillaries and venules.

Macular edema is an important and complex component of Non proliferative diabetic retinopathy (NPDR) and Proliferative diabetic retinopathy (PDR) and is the major cause of impaired vision. This study focusses on the role of Fundus Fluorescein Angiography (FFA) and Optical Coherence Tomography (OCT) in diabetic macular edema and its management.

ANATOMY OF THE MACULA

Anatomically the macula is defined as that portion of the posterior retina that contains xanthophyllic pigment and two or more layers of ganglion cells. The macular region is a specialised area of the central retina with a diameter of 5.5 mm and is centered approximately 4 mm temporal to and 0.8 mm inferior to the centre of the optic disc.

This area can be divided into several regions: the foveola, fovea, parafoveal area and perifoveal region. The central portion of macula contains the fovea and the foveola is a small depression in the internal surface of retina measuring about 0.35 mm in diameter. The fovea is located about 4mm temporal and 0.8mm inferior to the centre of optic disc.

The thickness of retina in the fovea is 0.13mm elsewhere it is 0.37 mm.The only photoreceptors in the fovea are cones. The inner nuclear, inner plexiform,ganglionic cell layer, nerve fibre layers are absent in the fovea. The entire vascular supply to the fovea is via the choriocapillaries. The maximal thickness of the retina is at the foveal margin is 0.55 mm and minimal thickness is at the umbo 0.13 mm.

At the macula ganglion cells are more numerous than anywhere else in the retina. The outer plexiform layer has a reticular structure but at the macula it is called the Henle ‘s layer. The fibres run at first vertically, then obliquely near the macula and finally parallel to the surface. This layer is thickest at the macula and absent at the fovea. There are no rods in the fovea. [2,3]

PARAMETERS OF MACULA

The diameter of fovea	-	1.5 mm
The diameter of parafovea	-	2.5 mm
The diameter of perifovea	-	1.5mm

PARAFOVEA:

It is a central annular zone which contain the largest number of nerve cells in the entire retina. The thickness of the photoreceptor layer in this portion of retina is 40 -45 microns.

PERIFOVEA:

The perifoveal retina is situated beyond the parafoveal area . There are 12 cones per each 100 microns in the perifoveal central retina.

UMBO

It is a tiny depression in the very centre of the foveola which corresponds to the foveal reflex, loss of which may be an early sign of damage.

BLOOD RETINAL BARRIER:

The outer blood retinal barrier is formed by the Zona Occludens between retinal pigment epithelial (RPE) cells.The inner blood retinal barrier is formed by the tight junctions between retinal capillary endothelial cells.

VASCULAR SUPPLY

The outer one third of the retina are supplied by the choriocapillaries. The inner twothird ‘s of the retina are supplied by the central retinal artery and veins.The inner capillary network is located in the ganglion cell layer and the outer in the inner nuclear layer. Capillary free zones are present around arterioles (periarteriolar capillary – free zone and at the fovea (Foveal avascular zone).[4]

Retinal capillaries are devoid of smooth muscle and elastic tissue and their walls consist of the following:

1. Endothelial cells form a single layer on basement membrane and are linked by tight junctions that form the inner blood retinal barrier.

2. Pericytes lie external to the endothelial cells and have multiple pseudopodial processes that envelop the capillary. They have contractile properties and are thought to participate in autoreulation of microvascular circulation.

HISTOLOGY

Based on light microscopic findings the retina is said to be composed of ten layers.These from outside to inside are:

1. The pigmented epithelium
2. The rods and cones
3. The external limiting membrane
4. The outer nuclear layer
5. The outer plexiform layer
6. The inner nuclear layer
7. The inner plexiform layer
8. The ganlionic cell layer
9. The nerve fibre layer
10. The internal limiting membrane

EPIDEMIOLOGY

The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR)[5] is a study on the progression of diabetic retinopathy.The duration of diabetes was directly associated with an increased prevalence of diabetic retinopathy in people with type 1 and type 2 diabetes.After 20 yrs of diabetes, nearly 99% of patients with type 1 and 60% with type 2 had diabetic retinopathy.

It is reported that 3% eyes with mild NPDR, 38% with moderate to severe NPDR, and 71% eyes with PDR develop Diabetic macular edema(DME). The incidence increases with advancing retinopathy.

CLINICAL ASSOCIATIONS AND RISK FACTORS

Diabetic macular edema(DME) severity is associated with

1. Diabetic retinopathy severity level

2. Duration of diabetes mellitus : Retinopathy in young patient with Type I DM does not develop for atleast 3-5 yrs after the onset of the disease. In type II DM it is difficult to determine the duration for the development of DR. In patients diagnosed before the age of 30 years, the incidence of DR after 10 years is 50% and after 30 years it is 90%.

DR rarely develops within 5 years of the onset of diabetes or before puberty, but about 5% of type 2 diabetics have DR at presentation.

3. Glycemic control : The Diabetes Control and Complication Trial(DCCT)[6] hyperglycemia causes breakdown of the blood retinal barrier by three major mechanisms : increased paracellular permeability of vascular endothelium, loss of endothelial cell integrity due to cell destruction, and increased transcellular transport through the endothelium. Type 1 diabetics appear to obtain greater benefit from tight control than those with type 2. Raised HbA1c is associated with an increased risk of proliferative disease.

4. Hypertension : Increased blood pressure increases the risk of progression of diabetic retinopathy. Tight control appears to be particularly beneficial in type 2 diabetics with maculopathy.[7,8]

5. Dyslipedemia

6. Nephropathy : If severe is associated with worsening of DR. Conversely, treatment of renal disease may be associated with improvement of retinopathy and a better response to photocoagulation.

7. Fluid retention

8. Pregnancy promotes the progression of DR. Predictating factors include poor pre pregnancy control of diabetes, too rapid control during the early stages of pregnancy, and the development of pre eclampsia and fluid imbalance.

9. Intraocular surgery

10. Uveitis

11. Panretinal photocoagulation

12. Anemia induced hypoxia causes the development of microanuerysms and other retinopathy changes.

13. Genetic factors : There has been found an increased risk of PDR in subjects with HLA (Human leucocyte antigen) DR4 and DR5 phenotype.

14. Ocular factors : Glaucoma reduced the severity and prevalence of DR.

PATHOPHYSIOLOGY

There are structural, rheological and biochemical factors that contribute to the development of DR

I. **Structural changes**

1. Capillary basement membrane thickening

2. Loss of microvascular intramural pericytes

3. Loss of endothelial cells

4. Endothelial cell dysfunction

II. Rheological changes

1. Platelet abnormalities like increased platelet adhesiveness, increased platelet aggregation, decreased platelet survival.

2. Red blood cell abnormalities like decreased deformability, increased rouleaux formation.

3. Incresed fibrinogen, alpha 2 macrogobulin and haptaglobulin

III. Biological changes

1. Prolonged hyperglycemia : Several sugars bind non enzymatically to protein forming advanced glycation end products which are long lived and play a causal mechanism for the diabetic complications.

2. Sorbitol pathway:

Sorbitol formed from glucose by Aldose reductase is converted slowly to fructose by sorbitol dehydrogenase.Since the later reaction is slow sorbitol builds up to toxic concentration leading to endothelial damage.

3. Increased level of Diacyl glycerol and Protein kinase C which causes decreased retinal blood flow.

4. Vascular Endothelial Growth Factor is a potent permeability agent responsible for DME.

CLINICAL PRESENTATION:

Patients with DME present with wide range of visual symptoms depening on the degree to which fovea is involved. Patients experience graual progressive vision loss, loss of colour vision, poor night vision, poor dark light adaptation.

Clinically DME has the following features

a. Thickening of macula

b. Blurring of the underlying choroidal vascular pattern

c. Loss of foveolar light reflex when foveola is involved

d. Cystoid spaces

e. Lipid exudation from the leaking microanuerysms in the form of ring known as circinate retinopathy.

CLASSIFICATION

It is divded into two subtypes Focal and diffuse macular edema.

Focal macular edema

Areas of focal leakage from microanuerysms and dilated capillary segments characterize focal macular edema. These areas of focal retinal thickness are delineated from the adjacent healthy retina by a complete or a partial ring of hard exudates

Diffuse Macular Edema

Diffuse macular edema results from the breakdown of blood retinal barrier with leakage from microanuerysms and dilated capillary bed throughout the posterior retina. It has a tendency to be bilaterally symmetrical. They may disappear spontaneously at the same time in both eyes even without laser treatment only to reappear later. Systemic factors like cardiovascular, renal diseases, systemic hypertension, or pre eclampsia may be associated with exacerbation and amelioration of diffuse macular edema.

The Early Treatment Diabetic Retinopathy Study(ETDRS)[9] criteria for clinically significant macular edema(CSME)

1. Thickening of the retina < 500 microns from the centre of the macula.

2. Hard exudates with thickening of the adjacent retina located 500 microns from the centre of macula

3. A zone of retinal thickening ,1 disc area larger in size located 1 disc diameter from centre of macula.

A simpler classification named **International Clinical Diabetic Macular edema** severity scale classified DME as :

Diabetic macular edema absent: No retinal thickening or hard exudates in the posterior pole.

Diabetic macular edema present: Some retinal thickening or hard exudates in the posterior pole.

Mild Diabetic macular edema: Retinal thickening or hard exudates in the posterior pole, but distant from the centre of macula.

Moderate Diabetic macular edema: Retinal thickening or hard exudates approaching the centre of macula but not involving the centre.

Severe diabetic macular edema: Retinal thickening or hard exudates involving the centre of macula.

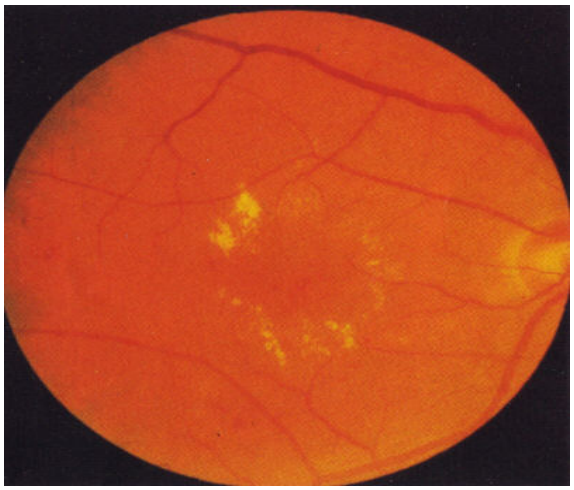


Fig.1 FOCAL EDEMA

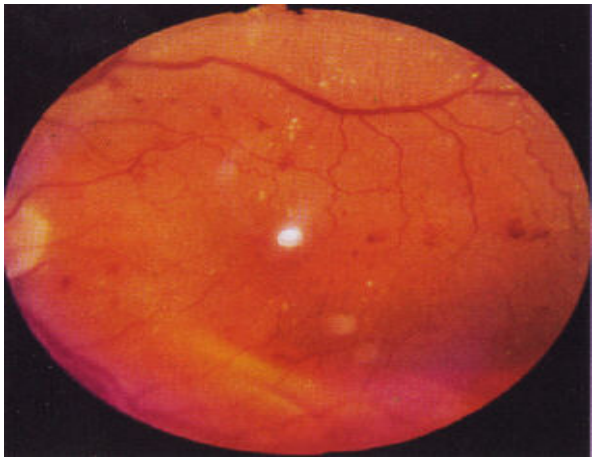


Fig. 2 DIFFUSE EDEMA

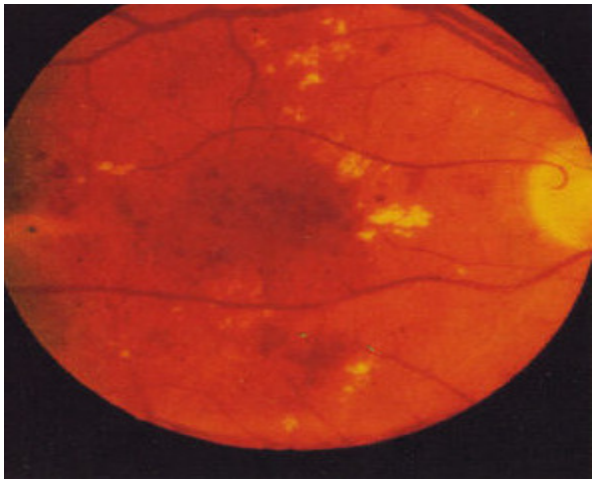


Fig.3 ISCHEMIC EDEMA

CLINICAL EVALUATION

1. Visual acuity

Vision loss depends on involvement of the macula.

2. Colour vision

Colour vision is documented by Fransworth Munsell 100 hue test. The commenest defect is blue yellow.In diabetes the sensitivity of blue cones are depressed.

3. Fields

Field charting by Tangent screen reveals scotomas corresponding to the areas of involvement in the fundus.

4. Indirect ophthalmoscopy

This technique allows the entire view of the entire retina.

5. Slit lamp biomicroscopy

6. Direct ophthalmoscopy

This method allows a detailed examination of the fundus with high magnification.

7. Threshold Amsler grid charting

This is useful in determining the central visual field.

8. **Photostress test**

After images and central scotomas persist after a long time. This explained the prolonged re-adaptation times in photostress testing the affected eye.

9. Electrophysiology

i. Electoretinography : Abnormalities of the oscillatory potential in the ascending limb of b wave and delay in implicit time occurs as the macular edema progresses.

ii. Electrooculography : Abnormal Arden ‘s ratio will be seen in DME

iii. Visually evoked potential : The VER shows reduction in amplitude with no change in latency.

10. Fundus fluorescein angiography

FFA is done for the diagnosis, documentation, identification of leakage pattern, decision on treatment and the follow up.

11. OCT

This is a valuable tool to diagnose, document, ascertain the macular thickness, decide about treatment and for the follow up.

FUNDUS FLUORESCEIN ANGIOGRAPHY

PRINCIPLES:

FFA is a tool for studying retinal vasculature. In 1910 the two medical students Harold Novotny & David Alvis produced the first human FFA. Fluorescein was chemcically related to phenolphthalein & in alkaline solution forms sodium fluorescein.It is a water soluble, orange red crystalline hydrocarbon. When injected into the body 80% is bound to the serum proteins and 20% remains unbound and is referred to as free fluorescein. Usual dose is 3ml of 20% in adults and 0.04ml/kg of 20% in children.

The retinal capillary endothelial cells are joined by special junctional complexes which make them impermeable to fluorescein and leakage from the retinal circulation is pathological. Major choroidal vessels are impermeable to both bound and free fluorescein but choriocapillaries are extremely permeable.

PHASES OF THE ANGIOGRAM:

1. Pre arterial phase or choroidal phase, during which the choroidal circulation is filling, but no dye has reached the retinal arteries.

2. Arterial phase , which follows one second after the pre arterial phase and extends from the first appearance of the dye in the arteries until the entire circulation has been filled.

3. Arterio Venous(AV) phase or the capillary phase which is characterised by complete filling of the arteries and capillaries with the appearance of early lamellar flow in the veins.

4. Venous phase which is subdivided according to the extent of venous filling and arterial emptying into early, mid, and late stages.

5. Elimination phase

TECHNIQUE:

Fluorescein, usually 5 ml of a 10% or in eyes with opaque media, 3ml of 25% solution is injected intravenously ino the antecubital vein over a few seconds images are taken at approximately 1 second intervals, 5-25 seconds after injection. Late photographs are taken after 10 minutes and occasionly 20 minutes if leakage is anticipated.

PATTERNS OF FLUORESCNCE

1. Hypofluoresence

Vascular filling defects and blocked fluorescence

2. Hyperfluorescence

Leakage, staining, pooling, transmission defect.

3. Autofluorescence

It is the appearance of fluorescence without dye injection due to normally fluorescent structures like drusen and lipofuscin.

4. Pseudofluorescence

It is due to mismatch of the filters in which filter fails to block unwanted light.

ADVERSE EFFECTS:

Discoloration of skin and urine, nausea, vomiting,, flushing of the skin, itching, and excessive sneezing. Serious but rare problems include syncope, laryngeal oedema, bronchospasm and anaphylactic shock.

DISADVANTAGES

1. Cannot be performed in hazy media

2. Cannot detect lesions under preretinal / subretinal hemorrhage.

CONTRAINDICATIONS

History of reaction to the dye

Severe renal or liver dysfunction

FFA CLASSIFICATION OF DME:

Focal Edema:

AV phase shows multiple hyperfluorescent points caused by microanuerysms bordering the areas of capillary non perfusion. Late phase shows increased fuzziness around the micoanuerysm due to leakage of the dye.

Diffuse Edema

Mid AV phase shows leakage of the dye from the dilated capillaries throughout the macula.It is not associated with hard exudates. FFA shows early spotty hyperfluorescence of microaneurysm and late diffuse hyperfluorescence due to leakage, and may be associated with a flower petal pattern if CME is present. Mostly bilaterally symmetrical. They may disappear spontaneously at same time in both eyes even without laser only to reappear spontaneously. The treatment is grid laser photocoagulation to areas of retinal thickening.

Ischemic type:

Retinal capillary nonperfusion is a feature commonly associated with progressive NPDR. Microanuerysms tend to cluster at the margins of capillary nonperfusion. Closure of retinal arterioles may result in a large area of capillary nonperfusion and progressive ischemia. Clinically the macula is normal. FFA shows enlargement of the foveal avascular zone greater than 1000µm in diameter. There does not appear to be a direct correlation between the level of visual acuity and the severity of ischemia.

It has the following features in FFA

1. Enlargement of Foveal Avascular Zone (FAZ)
2. Irreularities of FAZ
3. Capillary budding into FAZ
4. Widening of intercapillary space and capillary dropout in perifoveal area.

Treatment is not appropriate in most cases.

Mixed type:

Shows features of both diffuse type of macular edema. and ischemia.[10, 11, 12, 13]

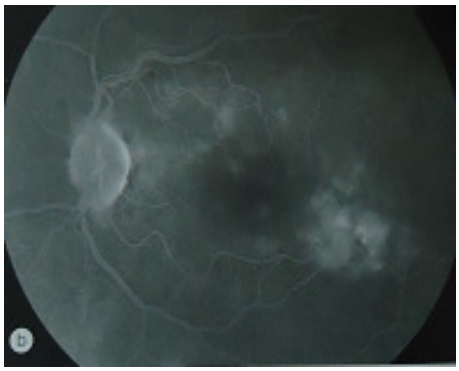


Fig.4 FOCAL TYPE

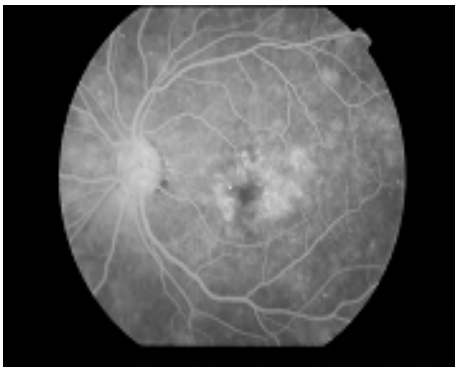


Fig.5 DIFFUE TYPE

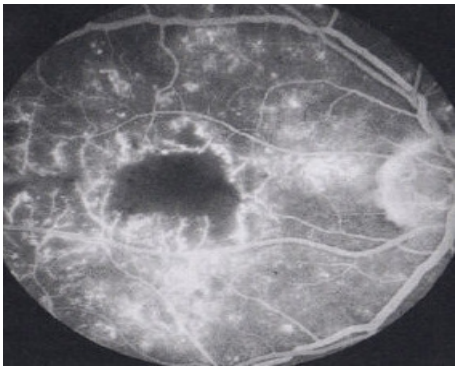


Fig. 6 ISCHEMIC TYPE

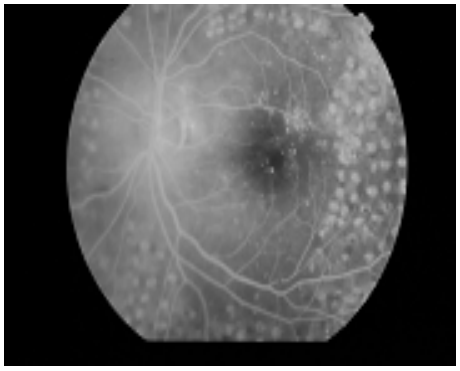


Fig.7 MIXED TYPE WITH GRID LASER MARKS

OCT

It provides a high resolution, cross sectional images of the macula and allows the measurement of foveal thickness. It also helped in determining the vitreo retinal relationship at the macula. OCT is superior to FFA in detecting cystoid changes. It captures reflected light from retinal structures to create a cross sectional image of the retina with an axial resolution of 15 microns.

PRINCIPLE:

It utilises interferometry and low coherence light in the infrared range (843 nm) to achieve high resolution(about OCT 1 & 2 & about 7 -8 microns for OCT 3), cross sectional imaging of the eye. An optical beam from a light source which emits short optical pulses or short coherence length light is directed into two beams, one is reflected and the other is transmitted.

Advantages to document the clinical efficacy of treatment compared to conventional FFA:

1. The 2 dimensional cross sectional OCT Scan allows detailed examination of macular anatomy distinguishing intraretinal, subretinal and cystoid fluid accumulation

2. The false colour image gives topographic image of the central fovea and perpendicular macular thickness.
3. The measurements are reliable, reproducible and observer independent.

TECHNIQUE:

Following papillary dilatation 6 radial scans are centered on the fovea.The retinal architecture is first displayed as a 2 dimensional image.

The retinal mapping program is employed to process the areas between 2 neighbouring scans in the periphery & determine the mean values of all 6 scans in the macula.

OCT SCAN PROTOCOLS IN MACULA :

1. Line scan
2. Radial scan
3. Macular thickness map
4. Fast macular thickness map
5. Raster lines
6. Repeat scan

ANALYSIS PROTOCOL:

1. Retinal thickness
2. Retinal map
3. Retinal thickness/Volume

INTERPRETATION:

Pathology categorised either as hyperreflective or hyporeflective lesion

Hyper reflective lesions

a. Hard exudates

b. Blood

c. Scars

Hypo reflective lesions

In the outermost ring than in the central zone.

a.Serous fluid

b. Hypo pigmented lesions of RPE

The OCT patterns in DME are

1.Sponge like retinal edema:

Thickening of the retina without definite cystic spaces. It is mostly confined to the outer plexiform and outer nuclear layers due to back scattering from intra retinal fluid.

2. Cystoid macular edema:

Cystoid cavities are hyporeflective spaces of various sizes mainly located in the outer retina.In long standing cases they fuse to form large cyst.

3. Serous retinal detachment:

Hypo reflective space under the fovea which may disappear spontaneously following laser.

4. Tractional macular edema:

Foveo vitreal traction causes detachment of fovea.It is an indication for Pars Plana Vitrectomy.

5. Taut Posterior Hyaloid Membrane:

It may cause recalcitrant macular edema with foveal detachment. [14, 15]

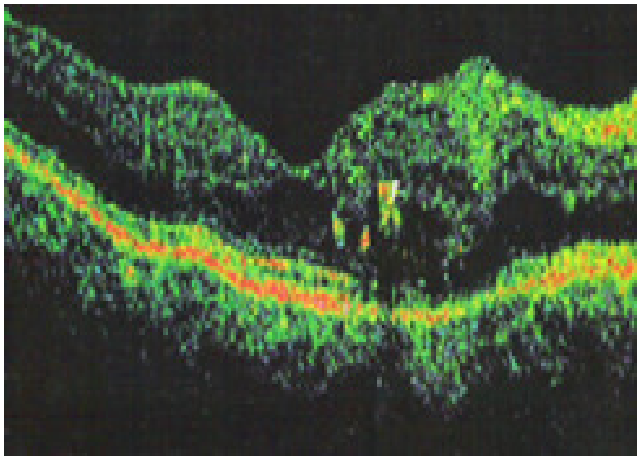


Fig.8 SPONGY EDEMA

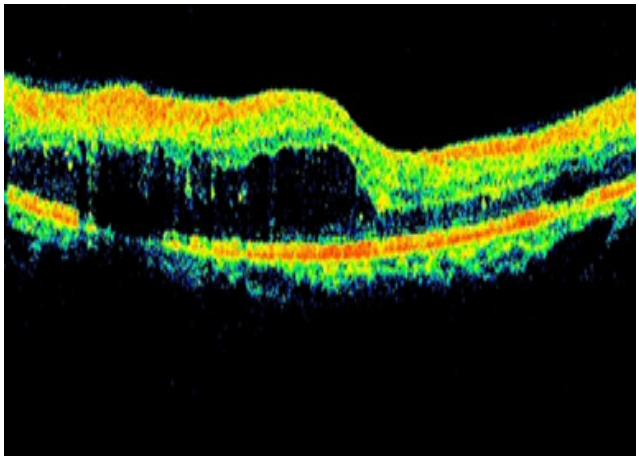


Fig.9 CYSTOID EDEMA

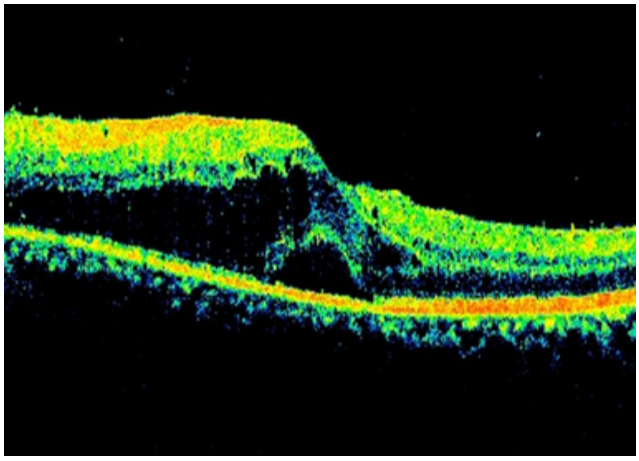


Fig. 10 SPONGY WITH SEROUS RD

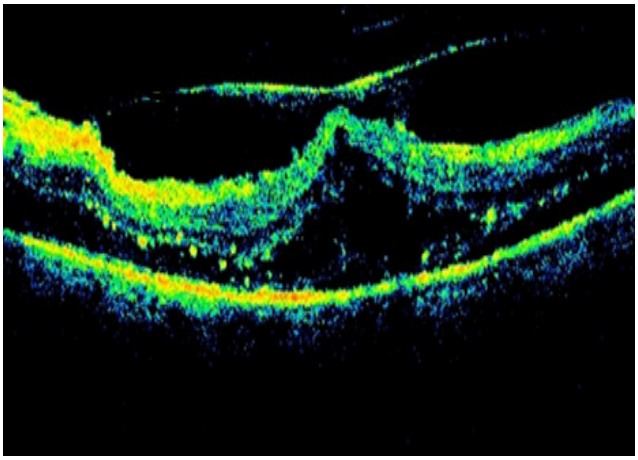


Fig.11 VITREOMACULAR TRACTION

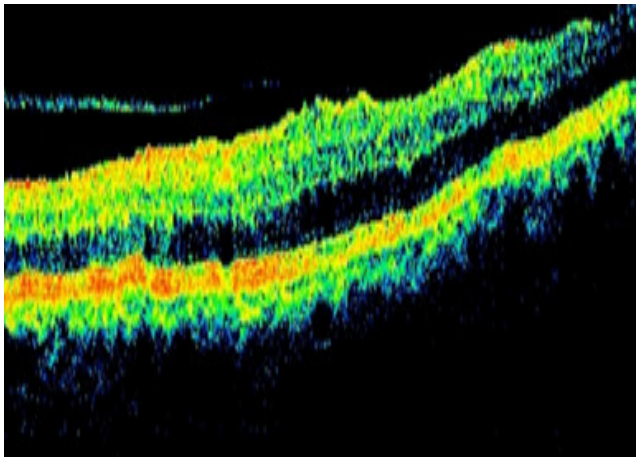


Fig.12 TAUT POSTERIOR HYALOID

LIMITATIONS AND PIT FALLS:

Retinal thickness in each zone is calculated as the average values measured on the portion of axis passing through that zone. Therefore there are fewer points per surface unit in the outermost ring than in the innermost ring therefore more values are extrapolated.

MANAGEMENT

Treatment strategies for DME encompasses life style modification exercise, smoking cessation, better control of blood sugar, blood pressure, blood lipids and body mass index.

PREVENTION AND CONTROL

Diabetes mellitus has multifactorial origin control of the metabolic abnormalities in diabetes has a major impact on the development and progression of diabetic microvascular complications. Diabetes Control and Complication Trial(DCCT) and the united kingdom prospective diabetes sudy (UKPDS)[16] have shown that optimal metabolic control could reduce the incidence and progression of DR. Multifactorial control of various risk factors such as HbA1c, blood pressure, lipid profile, anemia, 24 hrs proteinuria, before laser photocoagulation led to the reduction in macular edema on OCT. The

recommended values for HbA1c,blood pressure, and LDL cholesterol are <7 percent, <130/80 mmHg, and <100 mg/dl, respectively.

LASER THERAPHY FOR DME:

The goal of macular photocoagulation is to limit vascular leakage through a series of focal laser burns at leaking microanuerysms or grid laser burns in regions of diffuse breakdown of the blood retinal barrier. The ETDRS compared outcomes in eyes assigned to either deferral of macular laser photocoagulation or immediate treatment for CSME.

The ETDRS used focal laser photocoagulation for the treatment of DME. Results of the treatment with laser reduced the risk of moderate visual loss(defined as doubling of the visual angle eg. drop of 3 or more lines in Snellen s equivalent or a drop of 15 or more letters on ETDRS visual acuity chart), increased the chance of visual improvement and was associated with only a minor loss of visual field.[17]

TREATABLE LESIONS

1. Focal leaks > 500 microns from macular centre causing thickening or hard exudates.

2. Focal leaks within 300-500 microns from macular centre thought to be causing thickening or hard exudates.

3. Areas of diffuse leakage from microanuerysms and capillary leakage

4. Avascular zones other than Foveal Avascular Zone ,not treated previously.

Modified ETDRS Focal/Grid laser photocoagulation of DME

i. Lesions closer than 500µm from the fovea should not be treated.

ii. Excessive intense and excessive density laser burns should be avoided

iii. Intraretinal or preretinal hemorrhages should not be treated

iv. Consider treating large (>40µm) microanuerysms that appear to the principal causes of leakage focally to the ETDRS end point of colour change(either whitening or darkening).

TECHNIQUE OF FOCAL LASER

Focal refers to direct treatment of all leaking microanuerysms in the edematous retina between 500-3000 microns from the centre of the macula with a spot size of 50-100 microns and exposure time of 0.1 second.

TECHNIQUE OF GRID LASER

The grid laser is used primarily for areas of diffuse leakage with no identical focal areas of leakage. It consists of light intensity burns 50 -100 microns in diameter, producing a grid of equally spaced burns, more than one burn width apart..

LASER TYPES

Most frequently used wavelength are 514nm(the green component of the Argon Blue/Green laser) &810nm(from the infrared diode laser). The Argon blue green laser should not be used for the treatment of microanuerysms that are very close to the central area. This is because the blue light is absorbed by xanthophylls pigment overlying parafoveal area, this can cause nerve fibre layer damage and parafoveal scotoma.

SIDE EFFECTS AND COMPLICATIONS

- Paracentral scotoma
- Transient increased edema/decreased vision
- Choroidal neovascularisation
- Sub retinal fibrosis
- Photocoagulation scar expansion
- Inadvertent foveolar burns.[18, 19, 20]

MEDICAL MANAGEMENT OF DME

INTRAVITREAL STEROIDS

The rationale for the use of steroids to treat DME is compelling. The molecular biology of diabetic vascular change includes leukostasis, endothelial decompensation and increased levels of proinflammatory cytokines. Steroids may be useful to treat diabetic macular edema because of anti-inflammatory effects which include decreased inflammatory cell activation, adhesion and growth factor signalling. Steroids have a direct effect on maturation of interendothelial cell junction and improved barrier properties. The duration of drug in the vitreous cavity approximates the duration of clinical effect(2-3 months for 4mg injection of triamcinolone).

In patients with refractory DME intravitreal steroids have been used. Intravitreal triamcinolone 4mg / 0.1 ml alone or in combination with laser therapy, has been has been the subject of multiple investigations of therapy for DME. Patients with a cystoid component to their ME respond better. Visual decline are often observed 4 – 6 months after injection. Repeated therapy is often limited by side effects. Side effects include intraocular pressure elevation, acceleration of cataract, endophthalmitis, retinal detachment.[21]

INTRAVITREAL ANTI VASCULAR ENDOTHELIAL GROWTH FACTORS (VEGF)

Angiogenesis formation is central to the pathology of proliferative diabetic retinopathy and is stimulated by factors such as VEGF in response to retinal ischemia. VEGF may induce inflammation by inducing intracellular adhesion molecule –1 (ICAM-1) expression and leucocyte adhesion. Anti VEGF agents restore the normal permeability of the blood retinal barrier.

Bevacizumab is a full length, recombinant, humanized, monoclonal antibody directed against VEGF. In cases of diffuse DME that failed other treatments, intravitreal injection of bevacizumab 1.25mg in 0.05 ml was associated with improved vision and decreased retinal thickness 12 weeks after the first injection. However the effect is transient and the injection needs to be repeated at 4-6 weeks interval.

Pegatinib sodium (Macugen) 0.3 mg/0.05 ml 3 injections at 6 week intervals and were followed for 36 weeks. Pegatinib is a anti VEGF pegylated aptamer, that specifically binds and neutralises VEGF165, has been tried in recalcitrant ME.

Ranibizumab(Lucentis) is an intravitreally injected, recombinant, humanized, monoclonal antibody fragment designed to actively bind and inhibit all isoforms of VEGF.Complications include endophthalmitis, cataract, vitreous hemorrhage.injection site bleeding and pain.[22]

PHARMACOTHERAPY

1. Aldose reductase inhibitors – Sorbinil,Ponalrestat,Tolrestat Aldose reductase enzyme facilitates the conversion of glucose to sorbitol.They slow the development of diabetic retinopathy.

2. Advanced Glycation End Products inhibitors

3. Protein kinase inhibitors – Ruboxistaurin Protein kinase C ß is specifically upregulated in hyperglycemia in tissues like vascular endothelial cells, and mediates some of the myriad biochemical disturbances. Ruboxistaurin decreased abnormal vascular permeability and also inhibited angiogenesis in nondiabetic retinal ischemia model.

4. Antioxidants : The formation of reactive oxygen species(ROS) had been known to cause the development of diabetic complications. Diabetes may cause ROS production through glucose auto oxidation, increased flux through the polyol pathway, and increase in protein glycation.

Inhibition of superoxide production can effectively block sorbitol accumulation, AGE formation, and PKC activation.

SURGICAL MANAGEMENT OF DME

Pars plana vitrectomy and detachment of posterior hyaloid is useful in treating DME when there is evidence of posterior hyaloidal traction and taut posterior hyaloid. The Diabetic Retinopathy Vitrectomy Study (DRVS) was established to explore the possibilities and outcomes of vitrectomy in selected eyes. The results suggest that early vitrectomy should be considered in eyes with recurrent vitreous hemmorhage. Additional indications include traction of the disc, peripapillary retina or macula that distorts these structures and lead to reduction in vision, opaque fibrous proliferation in front of the retina and extensive pre retinal hemorrhage.

Vitrectomy with or without membrane peeling of posterior hyaloid membrane may be beneficial for the treatment of DME in eyes that are resistant to laser photocoagulation.[23]

PART TWO

AIM OF THE STUDY

i. To study the prevalence of diabetic maculopathy in relation to age, gender, duration of diabetes mellitus.

ii. To classify diabetic maculopathy using FFA & OCT

iii. To treat diabetic maculopathy according to FFA & OCT classification.

iv. To monitor the response to treatment with OCT.

MATERIALS AND METHODS

This study was conducted in Regional Institute of Ophthalmology And Government Ophthalmic Hospital, Egmore, Chennai from November 2009 to November 2011 for a period of 24 months.

INCLUSION CRITERIA:

All patients with clinically significant macular edema and with central subfield macular thickness more than 200 microns.

EXCLUSION CRITERIA:

i. History of severe systemic disease/steroids

ii. Uncontrolled Diabetes mellitus/Hypertension

iii. Any condition affecting follow up.

iv. History of associated glaucoma/ocular hypertension

v. History or evidence of ongoing uveitis

vi. Advanced diabetic eye disease

All the patients were taken a brief history and subjected to detailed systemic and ophthalmic examination. Anterior segment examination with slit lamp biomicroscope and posterior segment examination using 90 D, binocular indirect ophthalmoscope. Fundus photograph was also taken for documentation. Fundus fluorescein angiography, Optical coherence tomography were done for all patients.

Focal Photocoaulation was done for focal leak at peri and parafoveal area signifying macular edema. Direct treatment of leaking microanuerysms, were carried out with 50 to 100µ spot size of Nd Yag laser for 0.05 to 0.1 sec to produce mild to moderate burns.

Grid pattern photocoagulation was done for diffuse leak with 50 to 100µ spot size for 0.05 to 0.1 sec. Modified grid (Both focal and grid laser) were done for patients with mixed type of maculopathy. Ischemic maculopathy associated with ischemia elsewhere in fundus were given scatter photocoagulation and kept under observation.

Patients with Cystoid macular edema in OCT and refractory diffuse DME unresponsive to focal/diffuse laser photocoagulation were treated with intravitreal injection of Triamcinolone acetonide (4 mg/0.1 ml). Pre& post treatment follow up was done with OCT to find the treatment response. Patients with Vitreomacular traction (VMT) and Taut posterior hyaloid (TPH) patterns in OCT were planned for vitrectomy.

INTRAVITREAL injections procedure:

Injection procedure guidelines include consideration of pre existing conditions such as active external infection, eyelid abnormalities, povidone iodine, lid scrubs, preinjection topical antibiotics, lid speculum, drape, gloves, topical anaesthesia and post injection topical antibiotics. The risk of endophthalmitis following intravitreal injection is estimated to be approximately < 0.1%.

Guidelines for intravitreal injection:

Draping the ocular surface, eye lid, and eye lashes with povidone iodine, usage of lid speculum and avoidance of contamination of the needle with eye lid margin. Pupil should be dilated, topical anaesthetic drops should be applied before injection. Intraocular pressure(IOP) should be checked following injection.

FOLLOW UP:

Patients were followed up after 4 th,8 th & 16 th week, following laser photocoagulation. Following intravitreal injection patients were followed up on the immediate day following injection. They were followed up every week for 1 month, then every 2 weeks subsequently upto 6 months.

Main outcome measures:

1 .Best corrected visual acuity before & after treatment(Snellen's chart)

. 2. Macular thickness by OCT.

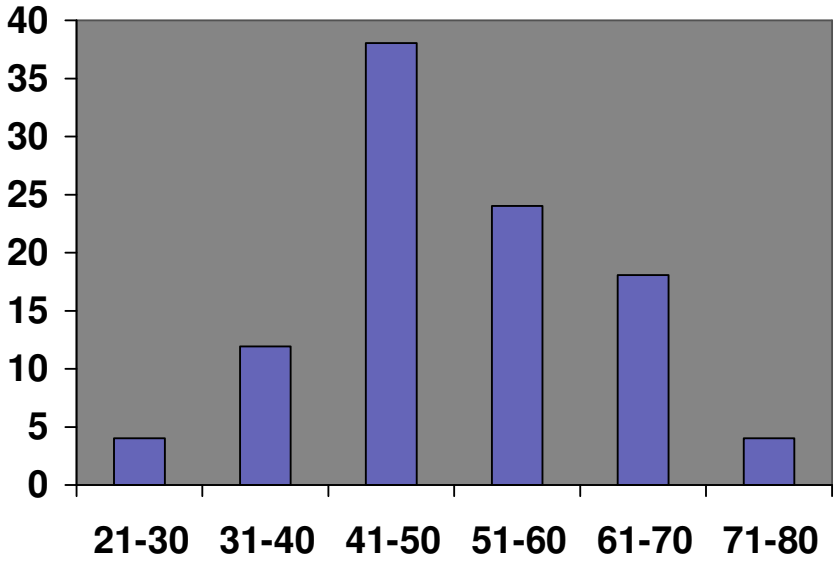
3. IOP should be measured by Goldmann 's applanation tonometry.

OBSERVATION AND ANALYSIS

1. AGE DISTRIBUTION

Table 1

Age group(years)	No of patients	Percentage
21 - 30	2	4%
31 - 40	6	12%
41 - 50	19	38%
51 - 60	12	24%
61 - 70	9	18%
71 - 80	2	4%

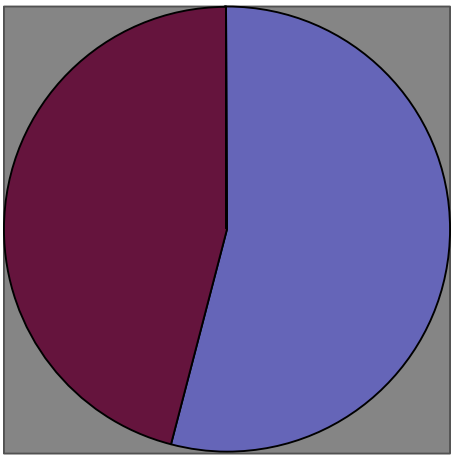


In our study the predominant age group affected is the 41-50 years range 38% followed by 51-60 years range 24% and 61-70 years range 18%. In our study 60% of cases are aged between 41-60.This correlates with the Wisconsin Epidemiological study [5]of Diabetic Retinopathy revealed diabetic retinopathy more prevalent in the middle aged population affecting people aged 41-60 years.

2. SEX DISTRIBUTION

Table 2

Sex	No. of Cases	Percentage
Male	27	54%
Female	23	46%

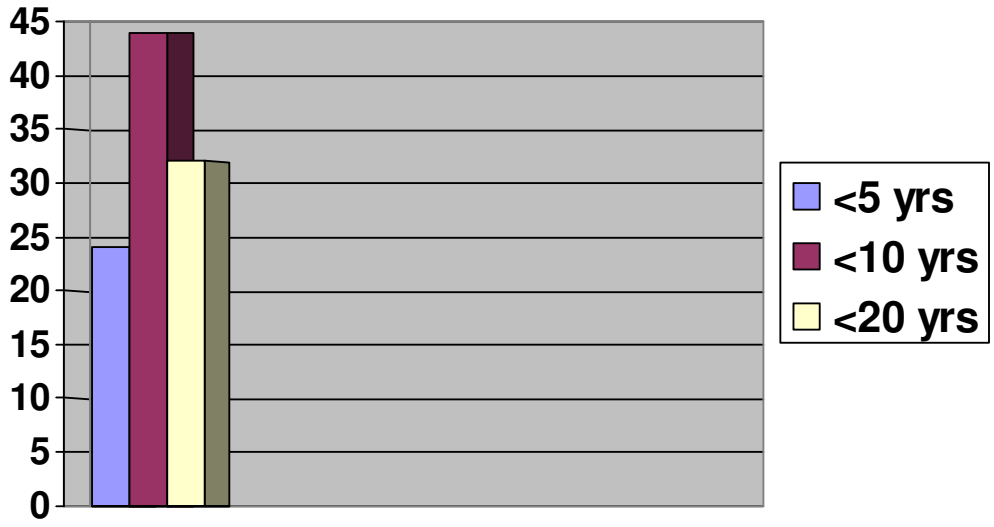


In our study, males were predominantly affected (54%) which correlated with the Wisconsin Epidemiological Study Of Diabetic retinopathy which showed a male to female ratio of 1.5:1.

3. DURATION OF DM

Table 3

Duration	No of patients with DME	Percentage of DME
<5 yrs	12	24%
5-10 yrs	22	44%
10-20yrs	16	32%

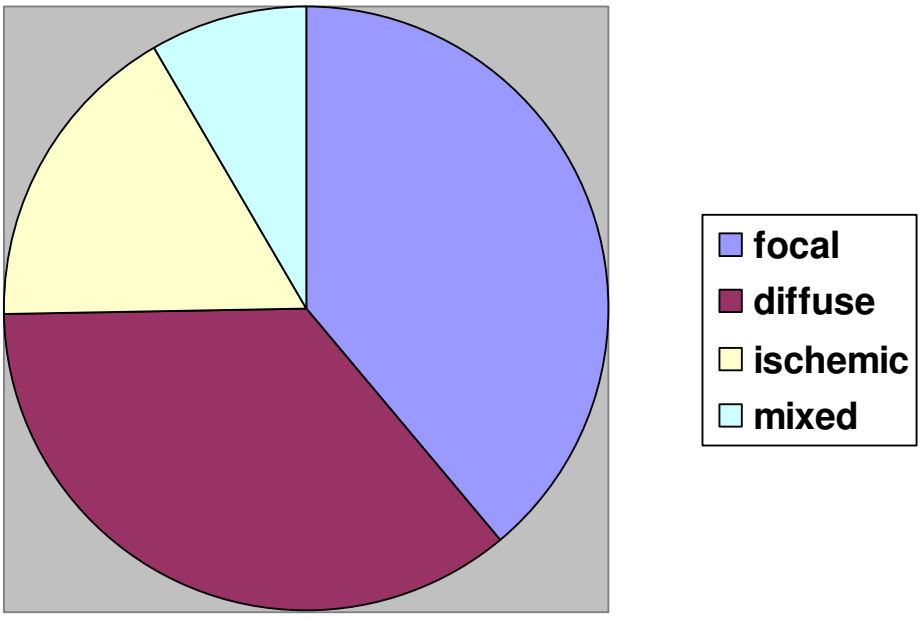


1. In our study though the incidence of DME with duration of <5yrs was 24%
2. The incidence was 44% in patients with duration of 5-10 yrs
3. And the incidence of DME with duration of 10-20 yrs was 32%

4. FFA TYPES

Table 4

Type	No. of Cases		Total
Focal	18	25	43
Diffuse	17	12	29
Mixed	7	9	16
Ischemic	8	4	12

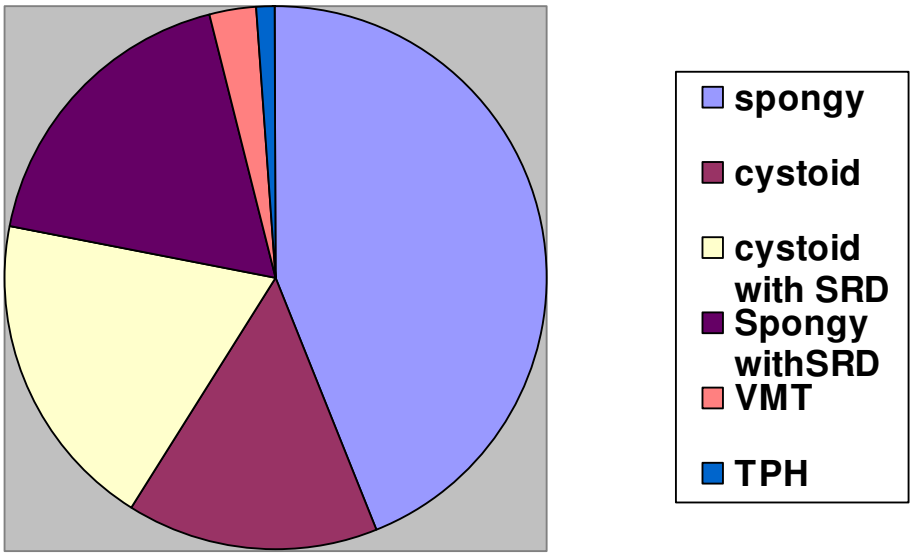


In our study 43 patients had focal type , 29 had diffuse, 16 had mixed type of maculopathy and 12 had ischemic maculopathy.

5. OCT TYPES

Table 5

Type	No of cases		Total
Spongy type	20	24	44
Cystoid type	9	6	15
Cystoid with serous RD	8	11	19
Spongy with serous RD	10	8	18
Vitreomacular traction(VMT)	2	1	3
Taut posterior hyaloid(TPH)	1	0	1



In our study 44 patients had spongy type in OCT, 15 had cystoid type,19 had serous retinal detachment with cystoid pattern, 18 had serous RD . VMT was seen in 3 patients and TPH in 1 patient. This correlated with the study done by Anush goyal et al which was presented in AIOC.[24]

6. TREATMENT

Table 6

LASER PHOTOCOAGULATION	48
IVTA	34

Laser photocoagulation was done in 48 patients. IVTA was given to 34 patients. 14 patients with ischemic maculopathy were kept under observation 4 patients with VMT and TPH patterns in OCT were planned for vitrectomy. But 2 patients were lost to follow up and 2 patients were not willing for surgery.

7. RESULTS of treatment in DME

Visual acuity on presentation

Table 7

Visual acuity	RE	LE	Total no of pts
<2/60	3	2	5
4/60-6/60	15	17	32
6/36-6/18	19	21	40
<6/12	13	10	23

40 patients had visusl acuity ranging from6/36-6/18 and 23 patients had visual acuity between <6/12. 48 patients were treated with laser photocoagulation & 34 were given injection IVTA. 18 patients with ischemic maculopathy were kept under observation . All patients were followed up over a period of 6 months.

8. Pretreatment visual acuity (Before laser & IVTA)

Table 8

Visual acuity	RE	LE	Total no of patients
<2/60	0	1	1
4/60 - 6/60	13	14	27
6/60 - 6/18	16	18	34
<6/12	9	20	20

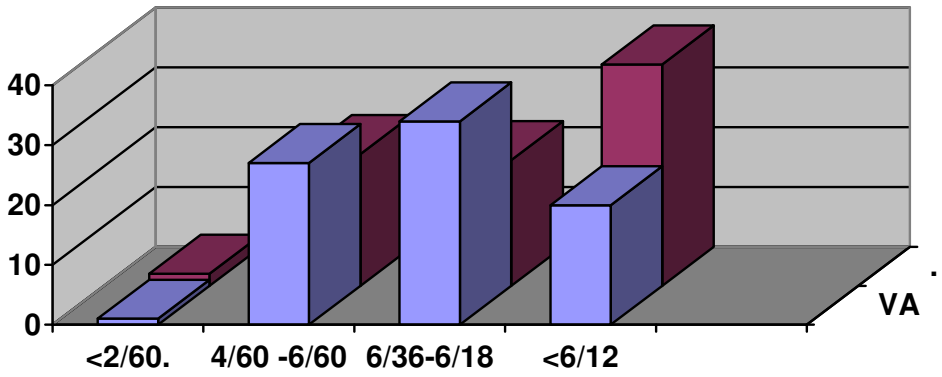
9. Post treatment visual acuity (After laser & IVTA)

Table 9

Visual acuity	RE	LE	Total no of patients
<2/60	2	0	2
4/60-6/60	10	12	22
6/36-6/18	23	16	21
<6/12	16	21	37

Post treatment only 2 patients had visual acuity less than2/60. 37 patients had visual acuity less than 6/12. 21 patients had VA ranging from 6/36-6/18 which correlated with the study by Becker et al.[25]

COMPARISON BETWEEN PRE AND POST TREATMENT VISUAL ACUITY



The post treatment visual acuity showed an increase with 37 patients having a VA of < 6 / 12 compared to 20% in the same range before treatment. **Chi square test showed p value< 0.02** on comparing the pre and post treatment visual acuity which is significant.

10. Pre treatment IOP

Table 10

IOP (mmHg)	No of patients
10-12	7
11-13	15
14-16	10
17-19	2
>20	0

11. Post treatment IOP

Table 11

IOP(mmHg)	No of patients
10-12	4
11-13	16
14-16	8
17-19	3
>20	3

Most patients maintained their IOP within the normal range with 2-4 mmHg between the pre and post treatment . But 3 patients had IOP >20 mmHg who were treated with topical 0.5% Timolol eye drops. Their IOP normalised at the end of 6 months.

29. **Effect of laser photocoagulation on visual acuity(VA) after 6 months**

Table 12

Visual acuity after 4 months	No of patients	% of visual loss
Improved	31	64.5
Unchanged	12	25
Worsened	5	10.41

Following laser photocoagulation vision improved in 64.5%worsened, in 10.% which correlated with the study conducted by E G Danes et al, R G Petty et ea, E M Kohner et al.[26]

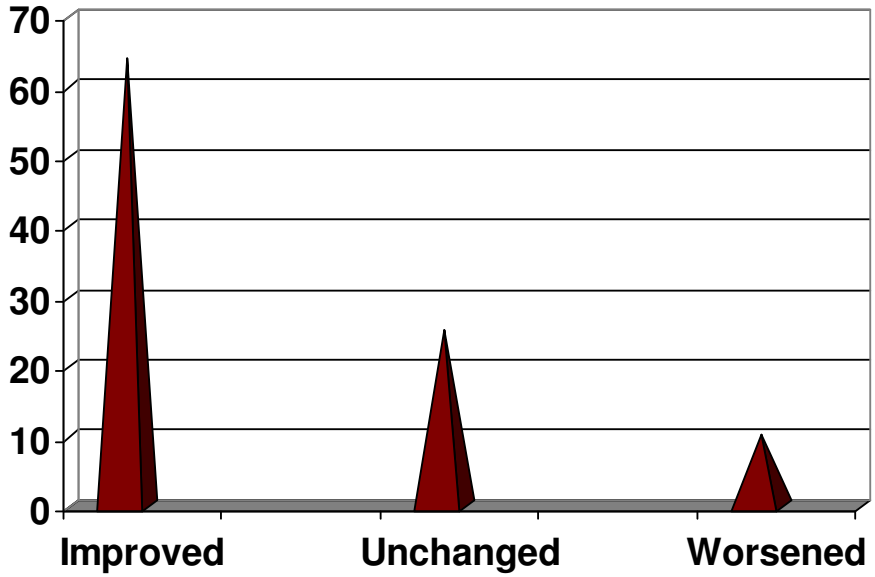
13. Effect of IVTA on VA after 6 months

Table 13

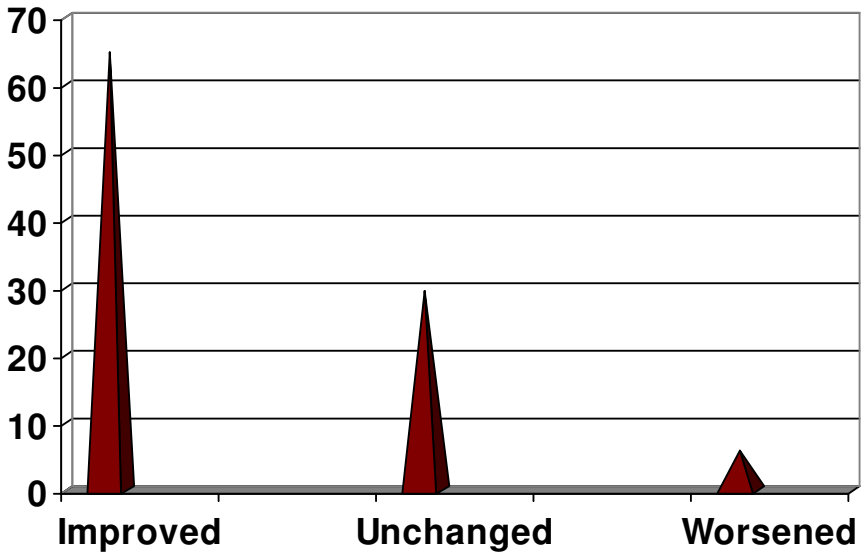
VA after 4 months	No of patients	% of visual loss
Improved	22	64.70
Unchanged	10	29.41
Worsened	2	5.88

Following IVTA vision improved in 64.70%, unchanged in 29%,worsened in 5%. Majority of the patients improved after IVTA injection which correlated with AmJ Ophthalmol 2005:140(4):695-702.[27]

V/A after 6 months of laser photocoagulation



V/A after 6 months of IVTA



14. PRE TREATMENT MACULAR THICKNESS(Before laser photocoagulation)

Table 14

Macular thickness(µm)	RE	LE	Total no of pts
200-400	15	10	25
400-600	4	8	12
600-800	6	3	9
800-1000	2	0	2

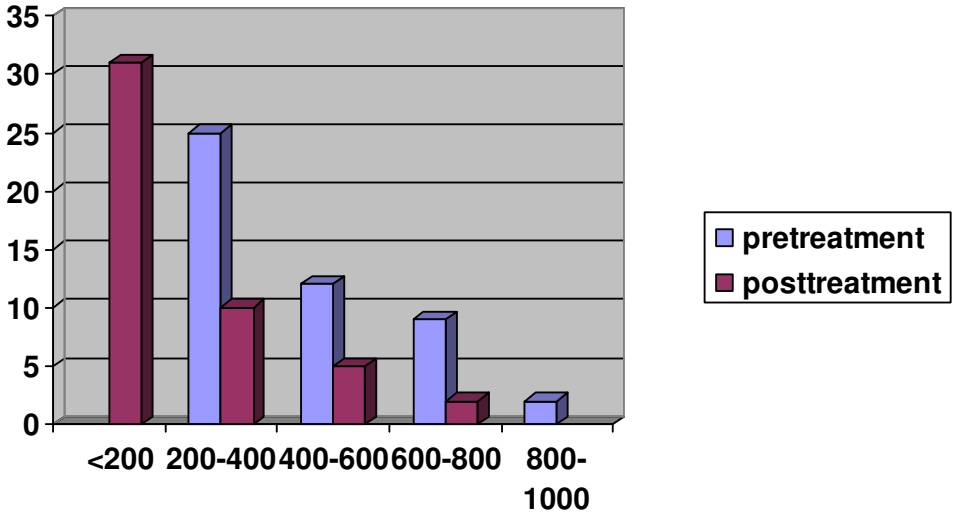
15. POST TREATMENT MACULAR THICKNESS(Following laser photocoagulation)

Table 15

Macular thickness	RE	LE	Total no of pts
<200	15	20	31
200-400	10	9	10
400-600	4	6	5
600-800	0	2	2

Pre treatment macular thickness was between 200-1000µ. 10patients had macular thickness between 200-400µ. Following laser treatment majority of patients had macular thickness less than 200µ which correlated with the ETDRS study.[9]

COMPARISON BETWEEN PRE AND POST TREATMENT MACULAR THICKNESS FOLLOWING LASER



Chi square test showed a p value <0.04% on comparing the pre and post treatment macular thickness which was significant.

16. Macular thickness in OCT pre & post treatment in FOCAL MACULOPATHY:

Table 16

Treatment	Decreased	Unchanged	Increased
laser	29	2	0
IVTA	11	1	0

17. Macular thickness in OCT pre & post treatment in DIFFUSE MACULOPATHY:

Table 17

Treatment	Decreased	Unchanged	Increased
Laser	9	0	1
IVTA	14	1	1

18. Macular thickness in OCT pre & post treatment in MIXED MACULOPATHY:

Table 18

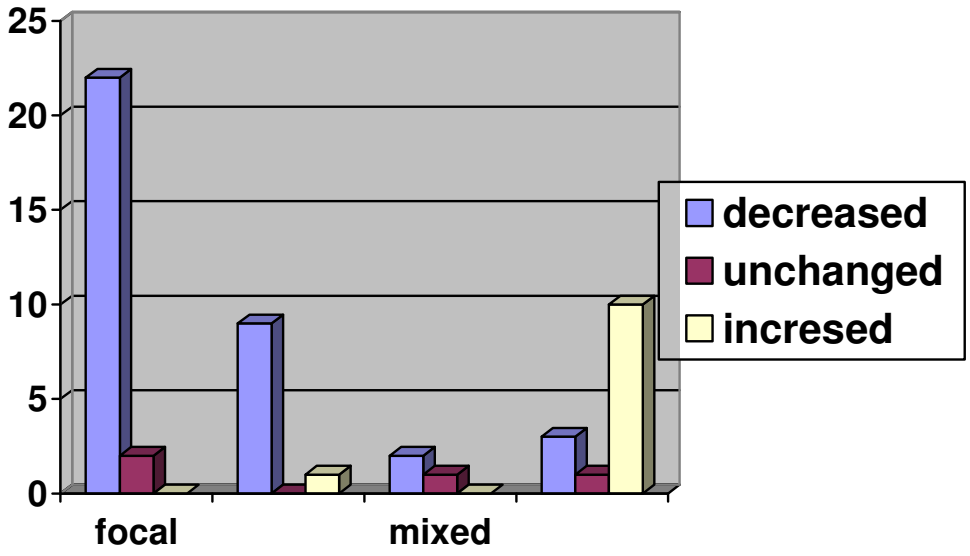
	Decreased	Unchanged	Increased
laser	2	1	0
IVTA	11	0	0

19. Macular thickness in OCT pre & post treatment in ISCHEMIC MACULOPATHY:

Table 19

Treatment	Decreased	Unchanged	Increased
observation	3	1	8

Macular thickness in OCT pre & post treatment in focal, diffuse and mixed maculopathy



Majority of the cases showed a decresease in macular thickness after treatment which was documented in OCT.

20. Macular thickness in OCT pre & post treatment in SPONGY EDEMA

TABLE 20

Treatment	Decreased	Unchanged	Increased
laser	33	3	8

21. Macular thickness in OCT pre & post treatment in CYSTOID EDEMA

Table 21

Treatment	Decreased	Unchanged	Increased
IVTA	**14**	**1**	**0**

22. Macular thickness in OCT pre & post treatment in CYSTOID EDEMA with SEROUS RD

Table 22

Treatment	Decreased	Unchanged	Increased
IVTA	18	0	1

23. Macular thickness in OCT pre & post treatment in SPONGY EDEMA with SEROUS RD

Table 23

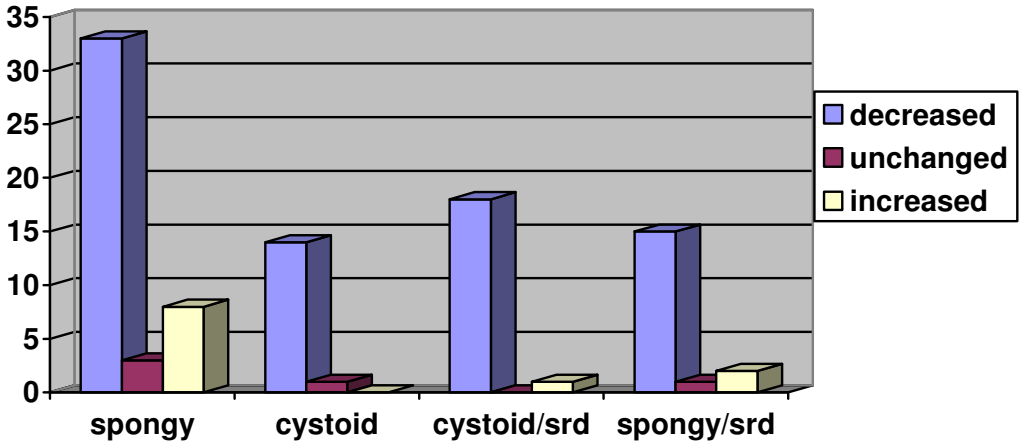
Treatment	Decreased	Unchanged	Increased
laser	15	1	2

24. Macular thickness in OCT pre & post treatment in VMT

Table 24

Treatment	Decreased	Unchanged	Increased
Observation(not willing for surgery)	0	0	2

Macular thickness in OCT pre & post treatment



Majority of the cases showed a decrease in macular thickness after treatment with laser / Inj IVTA.

25. Pre treatment macular thickness before IVTA

Table 25

Macular thickness	RE	LE	Total no
200-400 μ	6	4	10
400-600μ	10	5	15
600-800μ	4	3	7
800-1000μ	2	0	2

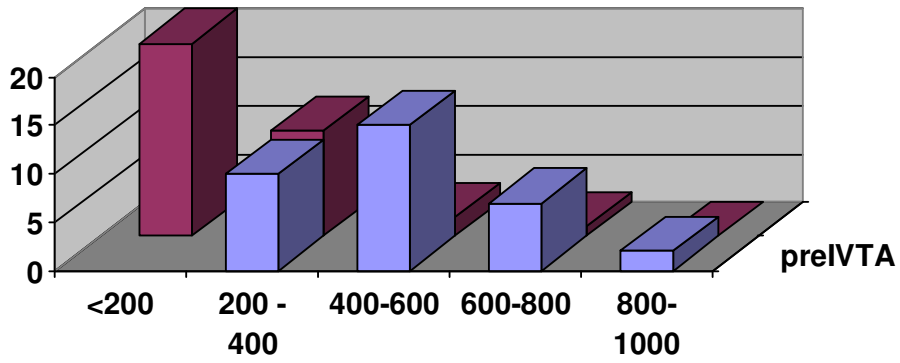
26. Post treatment macular thickness after IVTA

Table 26

Macular thickness	RE	LE	Total no
<200μ	9	11	20
200 - 400μ	7	4	11
400 - 600μ	2	0	2
600-800μ	0	1	1

The pre treatment macular thickness was between 200 to 1000μ. 10 patients had macular thickness between 200-400μ. 24 patients had macular thickness between 400 to1000μ. Post treatment all patients had macular thickness less than 600μ except one patient. 20 patients had reduced thickness <200μ which correlated with the study published in Br J Ophthalmol 2004, 88(9):1131-6.[28]

Comparison between pre and post treatment macular thickness after IVTA



Chi square test showed a p value,0.02 on comparing the pre and post reatment macular thickness after IVTA which was significant.

CASE 1

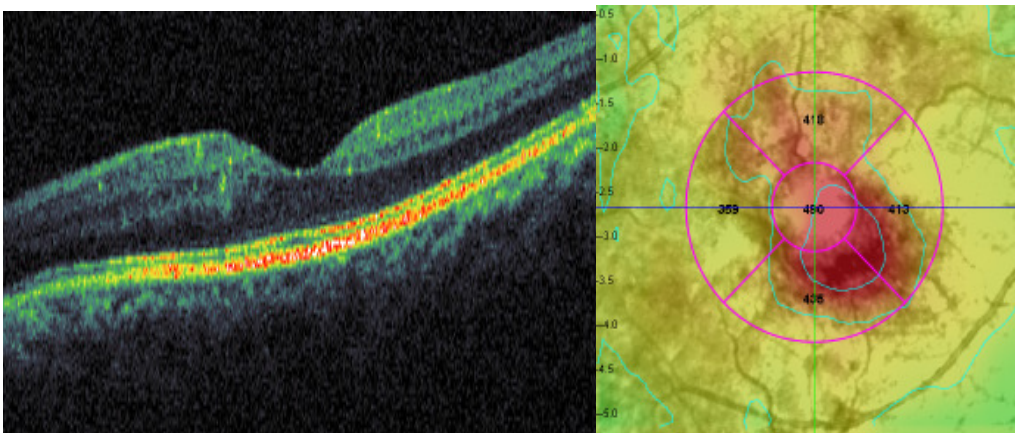


Fig. 13 OCT of the LE line scan showing spongy type of macular edema. Central macular thickness was 480µ

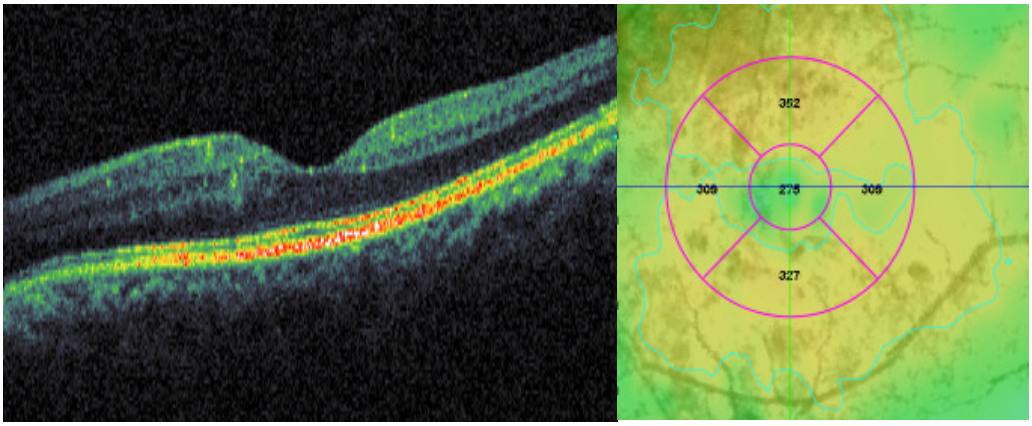


Fig 14. OCT LE after 24 weeks after laser treatment showing a reduction in the macular thickness to275µ

CASE 2

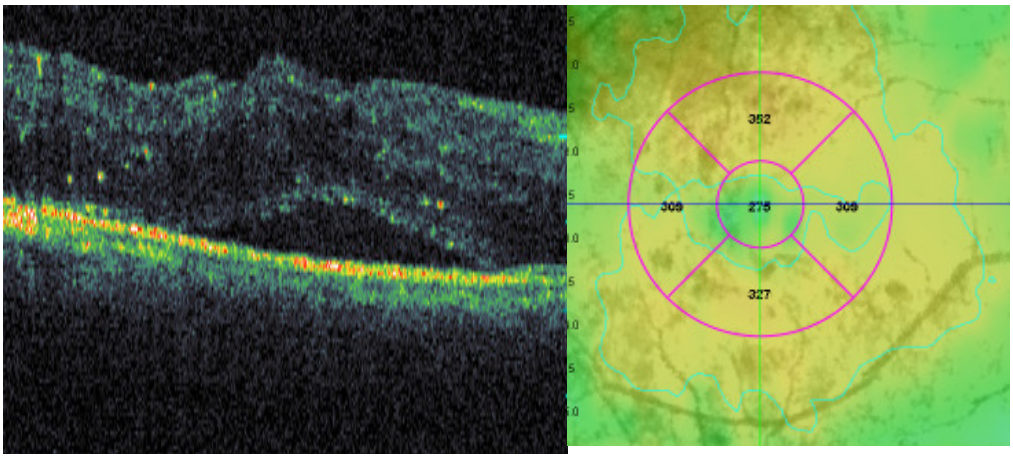


Fig 15. OCT RE line scan showed spongy edema with serous RD with central macular thickmess of 275µ

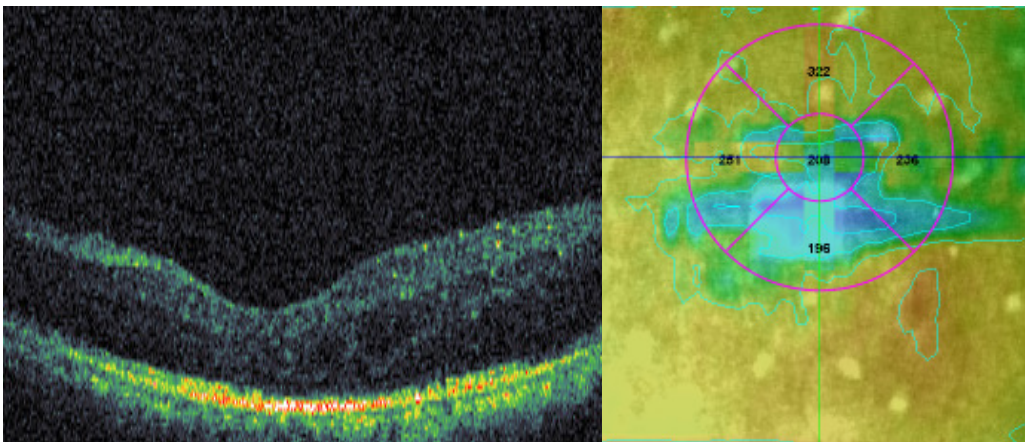


Fig. 16 OCT RE showed resolution of the serous RD with central macular thickness of 208µ after laser treatment

CASE 3

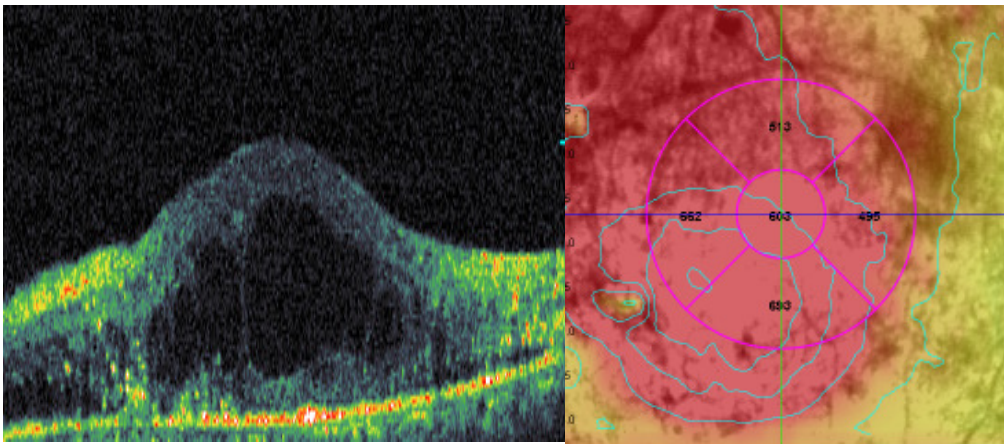


Fig. 17 OCT RE line scan showed cystoid type of macular edema with central macular thickness of 603µ

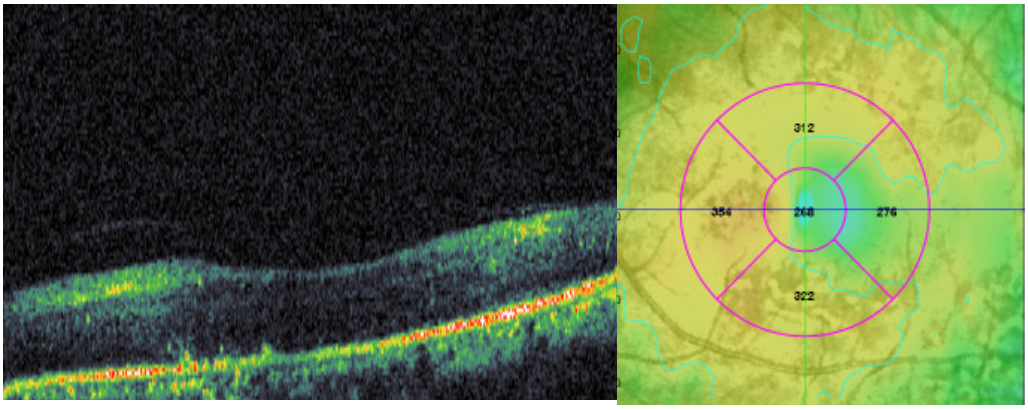


Fig 18 OCT RE line scan shows reduction in th ecystoid spaces with central macular thickness reduced to 260µ after injection IVTA

DISCUSSION

Diabetic macular edema is the major cause of visual morbidity in diabetic patients. The laser treatment given by ETDRS remains the standard therapy of DME. Focal and diffuse types of leaks diagnosed on FFA were treated with focal and grid laser. Cystoid type and recalcitrant type of macular edema not responding to laser treatment were given injection IVTA.

1 In our study 27 patients were below 50 yrs and 23 patients were above 50 years. This correlates with the Wisconsin Epidemiological study[5] of Diabetic Retinopathy and revealed diabetic retinopathy more prevalent in the middle aged population affecting people aged 41-60 years.

2. Males were predominantly affected around 54% which correlated with the Wisconsin Epidemiological Study[5] which showed a male to female ratio of 1.5:1.

3. 24% of patients had DME with 5 years duration, 44% with duration of 5-10 years, & 32% with duration of 10-20 years.

4. In FFA, 43 patients had focal type, 29 patients had diffuse type, 12 had ischemic type and 16 patients had mixed type of maculopathy.

5. In OCT classification 44 patients had spongy type, 15 patients had cystoid type, 19 patients had cystoid with serous RD, 18 patients had spongy with serous RD, 3 patients had VMT and 1 had TPH. This correlated with the study done by Anush goyal et al which was presented in AIOC[24]

6. 48 pts were treated with laser photocoagulation and 34 pts were treated with IVTA.

7. Only 2 patients had visual acuity < 2/60 and 37 patients had visual acuity < 6/12. which correlated with the study by Becker et al.[25] **Chi square test showed p value < 0.02** on comparing the pre and post treatment visual acuity which is significant.

8. After laser treatment 10 patients had macular thickness between 200- 400 μ and majority had macular thickness <200μ which correlated with the ETDRS study.[9] **Chi square test showed a p value < 0.04%** on comparing the pre and post treatment macular thickness which was significant.

9. Following IVTA 20 patients had macular thickness less than 200μ and all patients had macular thickness less than 600μ which correlated with the study published in Br J Ophthalmol 2004, 88(9):1131-6.[28]

Chi square test showed a p value, 0.02 on comparing the pre and post treatment macular thickness after IVTA which was significant.

10. Following laser photocoagulation VA improved in 64%, worsened in 25%, unchanged in 10 %. which correlated with the study conducted by E.G Danes et al, R G Petty et ea, E M Kohner et al.[26]

11. Following IVTA , VA improved in 64%, unchaned in 29%, worsened in 5%. which correlated with AmJ Ophthalmol 2005:140(4):695-702.[27]

12. Patients with ischemic maculopathy in FFA and VMT & TPH in OCT had the worst visual prognosis and their macular thickness was increased over the period of study.

CONCLUSION

In our hospital 100 eyes of 50 patients were studied during NOVEMBER 2009 to NOVEMBER 2011. The incidence of diabetic maculopathy is found to be commoner in the middle age group of 40-60 years the majority were males and the incidence of diabetic maculopathy increased with the increase in duration of diabetes.

Among the FFA patterns focal leaks were commoner and in OCT spongy edema were the common types. Patients who had ischemic type of maculopathy were kept under observation and had the worst prognosis over time. The majority of focal leaks improved with focal laser, and diffuse leaks with grid laser. And majority of recalcitrant types of macular edema and cystoid type showed improvement with IVTA injection. Patients with ischemic maculopathy in FFA and VMT & TPH in OCT had the worst visual prognosis

The overall improvement in visual acuity and the reduction in the macular thickness was detected and documented by OCT. FFA helped in detecting the specific leakage patterns and to decide the type of laser treatment. OCT aids in detecting subtle macular edema that may be difficult to detect on slit lamp biomicroscopy and in documenting the treatment response. and monitoring the response to treatment more accurately and less invasively than FFA. OCT & FFA play a major and complementary role in the diabetic maculopathy management and follow up.

PART THREE

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PROFORMA

Serial No

Name

Age

Sex

OP No.

Occupation

History

a. Complaints (RE/LE)
    i. Defective vision
    ii. Pain in the eye
    iii. Field defects

Past history:

i. Diabetes

Type

Duration

On oral hypoglycemics/inj insulin

ii. Hypertension

Duration

Medication

Family history

Systemic examination:

Pulse rate

Blood pressure

RBS

Urine alb & sugar

Ocular examination:

	RE	LE
Visual acuity	-	
Conjunctiva	-	
Cornea	-	
Anterior chamber	-	
Iris	-	
Pupils	-	
Lens	-	
Tension(applanation tonometer)	-	
Fields by Tangent screen	-	
Colour vision(Ishihara ‘s chart)	-	
Fundus examination	-	

By Direct Ophthalmoscopy

By Indirect Ophthalmoscopy

Fundus fluorescein angiography : Type of leak

Optical coherence tomography : Macular thickness

Tretment:

Laser photocoagulation:

Type (Focal/Diffuse/Modified Grid)

Power

Spot size

Number of burns

Injection IVTA:

Date

Follow up:

Visual acuity

Macular thickness

Name	Age	Sex	Diagnosis		VA pre treatment		FFA diagnosis		OCT diagnosis		Macular thickness pre treatment		Treatment done		VA after 6 months		Macular thickness after 6 months	
			RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE	RE	LE
gnanambal	56	F	mildNPDR/CSME	sevNPDR/CSME	6/36PH6/24	6/60NIP	mixed	focal	spongy	spongy	580	524	laser	laser	6/24PH6/12	6/60PH6/24	580	397
karunakaran	63	M	modNPDR/CSME	mildNPDR/CSME	6/36NIP	6/36PH6/12	focal	focal	Spongy with SRDSerousRD	cystoidwithSRD	284	289	laser	IVTA	6/36NIP	6/12PH6/9P	173	168
chinnayan	43	M	sevNPD/CSME	sevNPDR/CSME	4/60PH5/60	4/60PH5/60	diffuse	ischemic	spongy	spongy	456	621	laser	observation	4/60PH5/60	6/60NIP	320	642
gokila	28	F	mildNPDR	mildNPDR/CSME	6/24PH6/18	6/24PH6/12	focal	focal	spongy	cystoidwithSRD	226	354	laser	IVTA	6/12NIP	6/24PH6/18	193	187
elumalai	53	M	modNPDR/CSME	modNPDR/CSME	5/60NIP	4/60PH6/60	diffuse	diffuse	cystoid	cystoid	584	547	IVTA	IVTA	5/60PH6/60	6/60PH6/36	339	390
gubendran	45	M	mildNPDR	mildNPDR/CSME	6/24NIP	6/36PH6/12	focal	focal	cystoidwithSRD	Spongy with SRD	260	478	IVTA	laser	6/24PH6/12	6/24PH6/12	183	169
fathima	67	F	sevNPDR/CSME	sevNPDR/CSME	5/60PH6/60	5/60PH6/60	ischemic	mixed	spongy	spongy	586	784	observation	laser	6/60NIP	4/60PH5/60	591	561
srinivasan	58	M	mildNPDR/CSME	sevNPDR/CSME	6/12NIP	6/12NIP	diffuse	focal	cystoid	cystoidwithSRD	287	257	IVTA	IVTA	6/12NIP	6/24PH6/12	127	196
ranjitham	36	F	mildNPDR/CSME	modNPDR/CSME	6/36PH6/24	6/36NIP	focal	focal	spongy	spongy	210	264	laser	laser	6/24PH6/12	6/36PH6/18	182	197
george	47	M	sevNPDR/CSME	sevNPDR/CSME	6/60NIP	4/60NIP	mixed	focal	Spongy with SRDSerousRD	cystoidwithSRD	487	612	laser	IVTA	6/60PH6/24	5/60NIP	368	537
nagamani	58	F	sevNPDR/CSME	PDR/CSME	2/60NIP	3/60PH5/60	mixed	ischemic	TPH	Spongy with SRD	496	796	Patient lost to follow up					
dayalan	49	M	modNPDR/CSME	sevNPDR/CSME	6/60PH6/36	6/60PH6/18	diffuse	diffuse	spongy	cystoid	663	580	laser	IVTA	6/60PH6/24	6/60NIP	342	371
meena	41	F	mildNPDR/CSME	mildNPDR/CSME	6/24NIP	6/36PH6/12	focal	mixed	Spongy with SRDSerousRD	spongy	254	214	laser	laser	6/24PH6/12	6/24PH6/12	199	197
raju	29	M	mildNPDR/CSME	modNPDR	6/12NIP	6/12NIP	diffuse	focal	cystoid withSRD	cystoidwithSRD	226	256	IVTA	IVTA	6/12NIP	6/12PH6/9	167	189
pandian	54	M	modNPDR/CSME	modNPDR/CSME	6/60PH6/12	6/60PH6/24	mixed	diffuse	spongy	spongy	411	425	laser	laser	6/60PH6/24	6/60PH6/24	182	268
saraswathy	61	F	sevNPDR/CSME	sevNPDR/CSME	5/60PH6/60	5/60NIP	diffuse	ischemic	cystoid	songy	541	676	IVTA	observation	5/60PH6/60	5/60PH6/60	514	772
john	48	M	mildNPDR/CSME	sevNPDR	6/36PH6/12	6/12NIP	mixed	focal	Spongy with SRDSerousRD	cystoidwithSRD	352	364	laser	IVTA	6/36PH6/24	6/24NIP	184	147
padma	37	F	modNPDR/CSME	sevNPDR/CSME	6/36NIP	6/24PH6/18	focal	focal	spongy	spongy	298	241	laser	laser	6/36PH6/24	6/36PH6/12	175	186
prabakaran	42	M	modNPDR/CSME	sevNPDR/CSME	6/60NIP	6/60PH6/36	focal	mixed	cystoidwithSRD	cystoid	647	694	IVTA	IVTA	6/60NIP	6/60NIP	450	396
revathy	52	F	sevNPDR/CSME	sevNPDR/CSME	2/60NIP	6/60PH6/36	diffuse	focal	VMT	Spongy with SRD	854	498	Patient lost to follow up					
ravi	41	M	sevNPDR/CSME	modNPDR/CSME	6/60PH6/24	6/12NIP	ischemic	diffuse	Spongy with SRDSerousRD	spongy	497	291	observation	laser	6/60PH6/12	6/24PH6/18	490	165
shanthi	47	F	modNPDR/CSME	sevNPDR/CSME	6/60NIP	6/60NIP	focal	focal	spongy	cystoid	540	490	laser	IVTA	6/60PH6/36	5/60PH6/60	574	490
abraham	68	M	mildNPDR/CSME	modNPDR	6/24NIP	6/12NIP	diffuse	diffuse	cystoid	spongy	536	385	IVTA	laser	6/24NIP	6/12PH6/9	194	420
ramasamy	58	M	sevNPDR/CSME	sevNPDR/CSME	6/60NIP	6/60PH6/12	ischemic	focal	Spongy with SRDSerousRD	Spongy with SRD	471	412	observation	laser	6/60PH6/36	6/12NIP	512	189
gajalakshmi	34	F	modNPDR/CSME	sevNPDR/CSME	6/60NIP	6/60PH6/36	focal	focal	spongy	spongy	763	394	laser	laser	6/60NIP	5/60PH6/60	792	394
laksmipathy	43	M	sevNPDR/CSME	modNPDR/CSME	6/60PH6/36	6/36PH6/24	diffuse	focal	cystoid	Spongy with SRD	265	256	IVTA	laser	6/60PH6/36	6/36PH6/24	179	190
sekar	63	M	sevNPDR/CSME	PDR/CSME	2/60NIP	2/60NIP	mixed	focal	VMT	spongy	906	856	observation	laser	1/60NIP	4/60NIP	1023	587
gowri	49	F	modNPDR/CSME	modNPDR	6/60PH6/24	5/60PH6/60	focal	focal	spongy	Spongy with SRD	689	612	laser	laser	6/60PH6/24	5/60PH6/36	562	612
govindaraj	54	M	mildNPDR	modNPDR/CSME	4/60PH5/60	6/60NIP	diffuse	diffuse	cystoidwithSRD	Spongy with SRD	543	658	IVTA	laser	6/60PH6/36	6/60NIP	352	394
rajeswari	65	F	mildNPDR/CSME	modNPDR/CSME	6/12NIP	6/12NIP	focal	focal	spongy	spongy	268	246	laser	laser	6/12PH6/9	6/12PH6/9P	187	197
bagavathy	42	F	modNPDR/CSME	mildNPDR	6/36PH6/24	6/36PH6/12	diffuse	focal	cystoidwithSRD	cystoidwithSRD	348	414	IVTA	IVTA	6/36PH6/24	6/24PH6/18	198	171
arumugam	57	M	mildNPDR/CSME	modNPDR/CSME	6/60PH6/24	6/12NIP	focal	diffuse	Spongy with SRDSerousRD	Spongy with SRD	412	221	laser	laser	6/36PH6/24	6/12PH6/9P	185	188
palaniswamy	71	M	sevNPDR/CSME	sevNPDR/CSME	4/60NIP	4/60NIP	ischemic	focal	spongy	spongy	736	687	observation	laser	6/36NIP	6/12NIP	783	395
sundari	68	F	modNPDR/CSME	sevNPDR/CSME	5/60PH6/60	6/60PH6/36	diffuse	mixed	cystoid	cystoid	593	451	IVTA	IVTA	5/60PH6/60	6/36PH6/12	168	191
gopi	45	M	mildNPDR/CSME	mildNPDR/CSME	6/24NIP	6/36PH6/24	focal	focal	spongy	spongy	254	268	laser	laser	6/24PH6/12	6/24PH6/12	193	187
chinnaponnu	38	F	sevNPDR/CSME	sevNPDR/CSME	6/60NIP	6/60NIP	mixed	diffuse	cystoidwithSRD	cystoidwithSRD	621	881	IVTA	IVTA	6/60PH6/24	6/36NIP	397	886
andal	48	F	mildNPDR/CSME	mildNPDR/CSME	6/12NIP	6/12NIP	focal	mixed	Spongy with SRDSerousRD	spongy	217	231	laser	laser	6/12PH6/9	6/24PH6/9	172	190
marimuthu	54	M	sevNPDR/CSME	sevNPDR/CSME	4/60PH6/60	6/60NIP	ischemic	mixed	spongy	spongy	512	332	observation	laser	5/60PH6/60	6/60PH6/24	532	398
dhanam	42	F	modNPDR/CSME	mildNPDR	6/36PH6/24	6/24NIP	focal	diffuse	spongy	cystoidwithSRD	260	512	laser	IVTA	6/24PH6/12	6/36PH6/12	185	193
suburaj	65	M	mildNPDR	modNPDR/CSME	6/36NIP	6/12NIP	ischemic	focal	Spongy with SRDSerousRD	spongy	271	264	observation	laser	6/36NIP	6/24PH6/12	172	187
kalavathy	46	F	mildNPDR/CSME	mildNPDR/CSME	6/60PH6/24	6/36PH6/12	focal	mixed	cystoidwithSRD	spongy	692	264	IVTA	laser	6/36PH6/24	6/24PH6/12	164	196
paraman	52	M	sevNPDR/CSME	modNPDR/CSME	6/60NIP	6/60NIP	diffuse	ischemic	spongy	spongy	482	698	laser	observation	5/60NIP	6/36NIP	198	709
ayyadurai	74	M	modNPDR/CSME	modNPDR/CSME	6/60PH6/36	6/60PH6/18	focal	diffuse	Spongy with SRDSerousRD	cystoidwithSRD	417	546	laser	IVTA	6/24PH6/12	6/36PH6/24	196	186
bagyam	49	F	sevNPDR/CSME	sevNPDR/CSME	5/60PH636	5/60PH6/24	diffuse	ischemic	cystoidwithSRD	spongy	812	831	IVTA	observation	5/60NIP	6/36NIP	376	676
rajendran	39	M	mildNPDR/CSME	modNPDR	6/12NIP	6/60PH6/18	mixed	ischemic	spongy	spongy	214	690	laser	observation	6/24NIP	6/60PH6/36	497	690
banu	41	F	sevNPDR/CSME	modNPDR/CSME	5/60PH6/60	5/60PH6/60	diffuse	focal	cystoid	cystoidwithSRD	549	621	IVTA	IVTA	5/60PH6/60	6/60PH6/12	378	374
hariharan	51	M	sevNPDR/CSME	modNPDR/CSME	4/60NIP	6/60NIP	focal	mixed	cystoid	Spongy with SRD	487	456	IVTA	laser	6/60PH6/24	6/36PH6/24	169	314
kashthuri	48	F	modNPDR/CSME	sevNPDR/CSME	6/60PH6/18	6/60PH6/36	ischemic	diffuse	spongy	cystoid	487	635	observation	IVTA	6/60PH6/24	6/24PH6/12	260	335
muthu	62	M	sevNPDR/CSME	sevNPDR/CSME	4/60PH6/60	2/60NIP	diffuse	diffuse	cystoid	VMT	582	789	IVTA	observation	6/60PH6/36	1/60NIP	602	810
krishnaveni	43	F	mildNPDR/CSME	sevNPDR/CSME	6/36PH6/12	6/12NIP	diffuse	focal	spongy	spongy	461	412	laser	laser	6/12PH6/9	6/36PH6/12	196	183

KEY TO MASTER CHRART

VA	-	Visual acuity
NPDR	-	Non proliferative diabetic retinopathy
CSME	-	Clinically significant macular edema
FFA	-	Fundus fluorescein angiography
OCT	-	Optical coherence tomography
RE	-	Right eye
LE	-	Left eye
IVTA	-	Intravitreal Triamcinolone acetonide
VMT	-	Vitreomacular traction
TPH	-	Taut posterior hyaloid
CME	-	Cystoid macular edema