CHAPTER 2
RETINOPATHY IN DIABETES

Diabetic retinopathy is the major blinding ocular complication of diabetes, the overall prevalence of diabetic retinopathy varies in different populations, the highest prevalence being 54%. Diabetic retinopathy includes non-proliferative and proliferative retinopathy and the late sequelae of vitreous haemorrhage and tractional detachment. In developed countries, rates of blindness due to retinopathy range from 7.9% in diabetic patients younger than 65 years of age to 14.4% in those 65 to 74 years of age. The need for early identification and intervention is highlighted by the success of such programs as the Early Treatment Diabetic Retinopathy Study trials and the Diabetes Control and Complications Trial, which has asserted the need for tight glucose control.

Risk factors that modify the rate of onset and progression of retinopathy or the development of visual loss due to retinopathy have been studied, among these are duration of diabetes and blood glucose control. Increased duration of diabetes, increased fasting glucose levels, elevated systolic blood pressure, urinary albumin excretion, and decreased body mass index are independently associated with an increased risk for retinopathy.

Diabetic retinopathy is often accompanied by microvascular and macrovascular changes in other systems. Increased glucose levels are correlated with nephropathy, neuropathy, and cardiovascular complications.

We cannot overemphasize the need for early detection, good metabolic control, and early intervention in diabetes. Numerous studies have shown improved visual outcome and prevention of blindness with appropriate and timely intervention. To adequately inform the patients of the need for tight diabetic control is incumbent on physicians and other health care practitioners. Despite this, studies have shown that patient

information is poorly disseminated and that most patients are unaware of the importance of good metabolic control.

HISTORY:

- 1856 –V on Jager -first described diabetic retinopathy
- 1890 –Hirschberg -first classified & elaborated retinopathy
- 1943 - Ballantyne - Lowenstein -clinical and histological confirmation of diabetic retinopathy
- 1949-Gerd Meyer - Schwickerath -first recognised therapeutic effect of light on retina 1950- Jonas Friedenwald -histopathological characterisation of DRJ1
- 1953 –Aarseth - hereditary factors in diabetic retinopathy 1962 - Patz, Moumenee -micro aneurysms in a diabetic dog
- 1965- Engerman, - BloodworthMolitor -retinal changes in dogs rendered diabetic 1966-Gay, Rosenbaum -asymmetrical retinopathy in carotid insufficiency
- 1976-DiabeticRetinopathy - Study -preliminary report on effects of photocoagulation therapy
- 1984-Wisconsin - Epidemiologic Study-prevalence of diabetic retinopathy on Diabetic Retinopathy
- 1985-Early Treatment - Diabetic Retinopathy Study -effect of photocoagulation on diabetic macular edema
- 1985-DiabeticRetinopathy - Vitrectomy Study -effect of early vitrectomy for severe vitreous haemorrhage
- 1988-United Kingdom - Prospective Diabetic Retinopathy Study -effect of blood pressure and blood glucose on diabetic retinopathy
- 1993-Diabetes Control & - Complications Trial -effect of intensive control of blood glucose on retinopathy
- 1998-Klein -risk factors and progression of DR
- 2002-Marbidis, Duker -intravitreal triamcinolone for refractory diabetic macular edema.

RISK FACTORS

1. Level of glycaemic control
2. Serum lipids
3. Blood pressure
4. Duration of diabetes
5. Pregnancy
6. Renal disease and Coronary Artery disease

1. Level of glycemia

Hyperglycemia is a strong factor in the development and progression of diabetic retinopathy. Benefits of better control continue to manifest even after nonproliferative and proliferative diabetic retinopathy has developed. Elevated glycosylated hemoglobin (HbA1c) is a strong factor for the progression to high risk PDR. There is a 35% decrease in the risk of retinopathy progression for every 10% reduction in the presenting HbA1c level. The higher the level of HbA1c, the higher the risk of developing complications related to diabetes.

2. Serum lipids

Elevated levels of serum cholesterol are associated with increased severity of hard exudates. Elevated serum triglyceride levels are associated with an increased risk of developing high risk PDR and decreased visual acuity.

3. Blood Pressure

Intensive control of blood pressure slows down the progression of retinopathy and reduces the risk of other microvascular and macrovascular complications of diabetes mellitus. Abnormal systolic and diastolic blood pressures are associated with the severity of retinopathy in both type I and type II disease. In type I, both are important and in type II, only systolic BP is related to the progression of the retinopathy.

4. Duration of diabetes

Duration of diabetes is an important risk factor for the development of diabetic retinopathy After 20 years of diabetes, all the type I and > 60% of type II patients have some degree of retinopathy.

When age at diagnosis is <30 years

- <5 years of diabetes - retinopathy uncommon
- <10 years of diabetes: 1.2% have PDR
- >15 years of diabetes: 95% have some degree of retinopathy.
- >35 years of diabetes -67.2% have PDR

When age at diagnosis is >30 years

- <5 years of diabetes: 40% taking insulin have retinopathy
- >15 years of diabetes: 25% taking OHA have retinopathy 2% have PDR
- >25 years of diabetes: 53% taking OHA have retinopathy 25% have PDR

5. Pregnancy

Retinopathy progresses during pregnancy because of pregnancy itself or the changes in the metabolic control.

6. Renal disease and Coronary artery disease

Both are associated with increased incidence of proliferative retinopathy.

Sex Incidence

Male sex is associated with more severe retinopathy. The male : female ratio is 3:2.

Genetic Factors

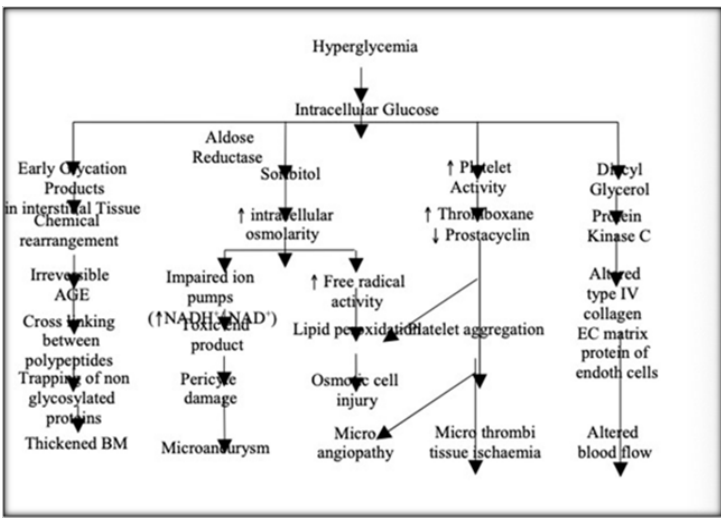
Relationship between HLA antigens expressed on the cell surface and the presence of retinopathy has already been documented. HLA – DR phenotypes 4/0, 3/0, and XX expressionis associated with increased proliferative retinopathy. Other HLA phenotypes conferring such increased risk include HLA B8, HLA B15 and HLA DR4.

Ocular Factors

Myopia reduces the prevalence and severity of diabetic retinopathy. Retinochoroidal scarring from trauma or inflammatory disease, reduces the prevalence of retinopathy by decreasing the retinal metabolism and thereby decreasing the need for oxygen and the release of vasoproliferative factors.

Pathogenesis

There is a complicate interplay of various factors in the pathogenesis of diabetic retinopathy.



I. BIOCHEMICAL MECHANISMS

1. Prolonged hyperglycemia

It is the major risk factor in the micro vascular complications of diabetes mellitus. Three mechanisms seem valid for diabetic retinopathy

i. Alteration in the expression of one or more genes resulting in increased amounts of altered gene products causing altered cell function.

ii. Non enzymatic glycation of proteins leading to cross linking and altered protein function. These products have very long cellular lifetime.

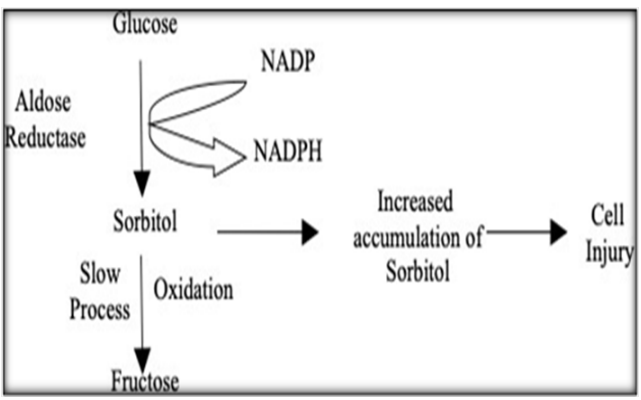
iii. Chronic hyperglycemia causes accelerated oxidative stress in cells resulting in toxic end products. Also increased activity of polyol pathway increases the

NADH/NAD+ ratio resulting in increased toxic end product, by a mechanism called hyperglycemic pseudo hypoxia.

2. Sorbitol Pathway

Aldose sugars are converted to their respective alcohol by the enzyme aldose reductase and again to their key to sugars by dehydrogenase.

Glucose is a relatively poor substrate for aldose reductase with high Km (binding constant). Under normal conditions, glucose is acted on by hexokinase to proceed on the glycolytic cycle.



In uncontrolled hyperglycemia, the hexokinase pathway gets saturated and glucose is acted upon by aldose reductase using NADP as cofactor, resulting in formation of excess sorbitol.

Further oxidation of sorbitol to fructose is a slow process resulting in building up of intracellular sorbitol leading on to cell damage and microvascular complications.

3. Diacyl glycerol and protein kinase C

Hyperglycemia causes an increase in diacyl glycerol which in turn activates protein kinase C which causes alteration in expression of type IV collagen and extra cellular matrix proteins of endothelial cells.

II. Rheological Mechanisms

- Abnormality of Platelets

Increased platelet adhesion, increased aggregation, increased factor VIII – Von Willebrand factor and decreased lifespan of platelets also play a role in retinopathy development.

- Abnormalities of Red Blood Corpuscles (RBC)

In diabetic individuals, there is increased rouleaux formation and reduced deformability of RBC. This is presumed to be due to altered α2 macroglobulin, haptoglobulin and increased fibrinogen.

4. Vascular endothelial growth factor (VEGF)

VEGF is associated with proliferative retinopathy and maculopathy. Hypoxia stimulates the release of VEGF from the retinal and optic nerve glial cells of diabetics.

Pathology

1. Capillary basement membrane thickening

Quantitative electron microscopic immunocytochemical studies show increased thickening of capillary basement membrane

with an increase in type IV collagen. Studies show along with thickened basement membrane, there is Swiss Cheese vacuolisation and fibrillar collagendeposition. Certain functions served by basement membrane are deranged in diabetes. They are:

- Structural rigidity to the blood vessels
- Filtration barrier for various molecules
- Barrier for vasoproliferation.

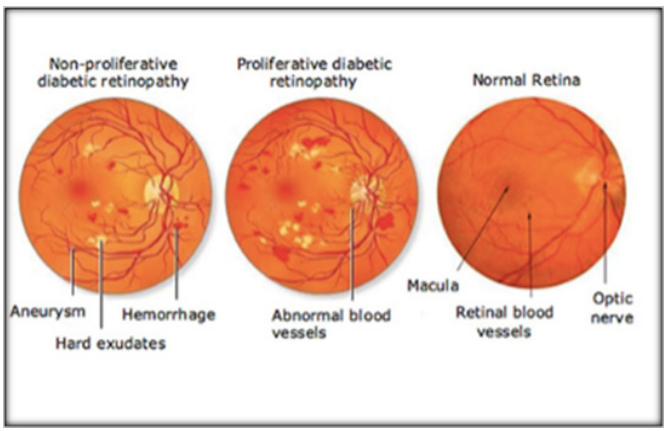


Image: showing different stages of retinopathy.

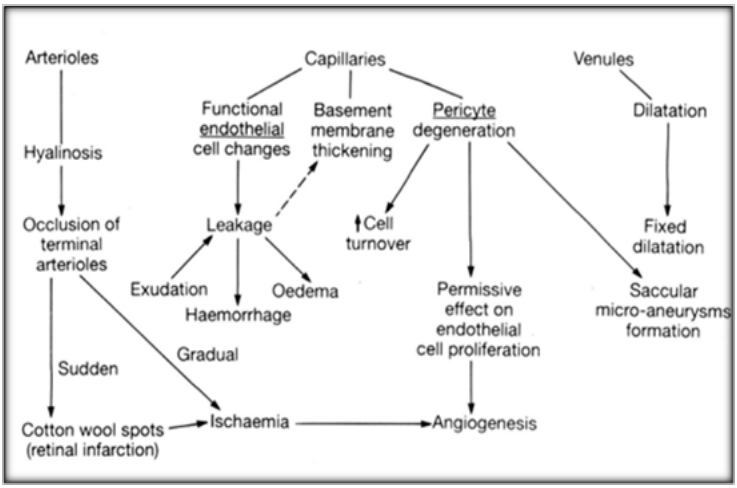
2. Loss of microvascular intramural pericytes

The capillary wall has pericytes surrounding the endothelial cells. Of these, pericytes have aldose reductase rather than endothelial cells. Hence more sorbitol gests accumulated in pericytes causing damage to them. The drop out of pericytes is recognized as empty, balloon– like space bulging from the capillary wall. Normal pericyte to endothelial cell ratio is 1:1. In diabetic retinopathy this ratio gets altered.

3. Microaneurysms

On trypsin digested retinal mounts, microaneurysms appear as hypercellular saccular outpouchings of capillary wall.

Microaneurysms may hyalinize and get occluded with PAS-positive material.



4. Capillary acellularity

Complete loss of all cellular elements from retinal microvessels.

5. Breakdown of blood-retinal barrier

Breakdown of blood-retinal barrier occurs due to:

- Opening of tight junctions (Zonulae occludentes) between adjacent microvascular endothelial processes.
- Fenestration of endothelial cell cytoplasm. Increase in transport by endocytic vesicles.

6. Exudates

Hard exudates: 14 Hard, yellow, waxy lesions

7. Neovascularisation

The growth of new vessels in retina either on disc or elsewhere.
Stage 1 : The stage of naked vessels.

Fine, new vessels without supporting connective tissue arising

from capillaries, grows in the plane of retina or invades vitreous.

Stage 2: The stage of condensation of connective tissue There is laying of connective tissue around the naked vessels which starts condensing.

Stage 3: The stage of cicatrisation

Gradual reduction in number and size of new vessels is associated with an increase in the connective tissue density. This on contraction forms sheets and bands on the retina.

Classification

Diabetic retinopathy is classified by Hirschberg as early as 1890. Later it was further classified by Ballantyne and Michaelson (1947 – 1962), Scott (1951), Alaerts and Slosse (1957) and Lee (1966). Duke Elder classified diabetic retinopathy as

1. Pre-retinopathy Stage

Decreased activity in ERG and EOG

2. Simple Diabetic Retinopathy

Appearance of microaneurysms, superficial and deep retinal haemorrhages, hard and soft exudates and vascular anomalies.

3. Proliferative Stage:Neovascularisation over the disc or elsewhere, vitreous haemorrhage and complications like retinal detachment can occur in this stage.

Early treatment diabetic retinopathy study (ETDRS) classifies nonproliferative diabetic retinopathy (NPDR) as follows

- Mild: at least one microaneurysm, microaneurysms or haemorrhages< standard photograph 2A
- Moderate:microaneurysms&haemorrhages> standard photograph 2A, soft exudates, venous beading and intraretinal microvascular anomalies (IRMA)
- Severe: any one of the following (4:2:1 rule) microaneurysms / haemorrhages in 4 quadrants or venous beading in >2 quadrants or IRMA in one quadrant.

- Very severe: any two or more of the above mentioned.

ETDRS classifies clinically significant macular edema as

1. Thickening of retina at / within 500 micron from center of the macula or
2. Hard exudates at / within 500 micron from center of the macula with adjacent retinal thickening or
3. zone of retinal thickening of one disc area or larger, a part of it is within, one disc diameter of the center of macula

Diabetic Retinopathy Study classifies proliferative diabetic retinopathy (PDR) as

- Early: New vessels on the disc / elsewhere
- High risk: New vessels over disc >1/3–1/4 disc area or New vessels over disc and preretinal or vitreous haemorrhage or New vessels elsewhere >1/2 disc area and preretinal or vitreous haemorrhage.

Studies on Diabetic Retinopathy

Early treatment diabetic retinopathy study (ETDRS)

This is a randomised clinical trial to ascertain the effect of laser in diabetic retinopathy. Results:

- Aspirin did not alter the progression of diabetic retinopathy or increase vitreous haemorrhage.
- Early PRP is not indicated in eyes with mild - moderate retinopathy.
- Early PRP resulted in reduction in the risk of severe visual loss.
- Focal photocoagulation for diabetic macular edema reduced the risk of moderate visual loss and increased moderate visual gain.

Diabetic Retinopathy Study (DRS)

This clinical trial evaluated the effect of PRP in diabetic retinopathy. Results :

- Xenon arc photocoagulation caused a > 50% reduction in the rates of severe visual loss (SVL).
- Treated eyes with high risk PDR achieved the greatest benefit.

United Kingdom Prospected Diabetic retinopathy Study (UKPDS)

This is a randomised control trial which was conducted to evaluate the effectiveness of intense control of blood pressure and blood glucose in type II diabetic patients.

Results: Intense control of blood pressure and blood glucose slowed the progression of retinopathy and reduced the risk of microvascular complications.

Diabetes Control and Complications Trial (DCCT)

This study was conducted with the aim to evaluate the effectiveness of intense control of blood glucose in type I diabetes.

Results:

- Intensive control of blood glucose reduced the risk of developing retinopathy by 76% and slowed the progression by 54%.
- It reduced the risk of neuropathy by 60% and nephropathy by 54%.

Diabetic Retinopathy Vitrectomy Study (DRVS)

This randomised prospective clinical trial investigated the role of vitrectomy in diabetic retinopathy.

Results: Early vitrectomy in type I diabetics had clear benefit

over deferral group, especially severe PDR benefited more.

Wisconsin Epidemiologic Study on Diabetic Retinopathy (WESDR)

This study depicted the prevalence and risk factors associated with diabetic retinopathy.

Clinical Features

I. Non proliferative diabetic retinopathy

The pathological processes in NPDR include retinal capillary micro aneurysm, increased vascular permeability and eventual capillary closure.

1. Microaneurysm

Meckanzie and Nettleship were the first to note microaneurysms. They appear as deep red dots varying from 15micron to 60 micron in diameter. It is most common in posterior pole and appears & disappears with time. Weakness of capillary wall, loss of pericytes, release of vasoproliferative factor, abnormalities of adjacent retina and increased intra luminal pressure play a role in its development.

2. Hard exudates

With progressing retinopathy, vascular permeability of retinal capillaries increases resulting in leakage of serum and lipids resulting in hard exudates and macular edema. Hard exudates are yellow - white intra retinal lipid deposits located at the border of edematous and nonedematous retina. They present as clusters, plaque and circinate / ring patterns.

3. Intra retinal haemorrhages

Superficial haemorrhages: Flame shaped due to the accumulation of blood in the superficial retinal layers parallel to the coursing nerve fibres.

Deep haemorrhages: Dot and blot in the inner nuclear and outer plexiform layers and its breaks through the confines of Muller cell processes.

4. Capillary closure

Capillary closure results in patchy areas of nonperfused retina with clusters of microaneurysms, cotton wool spots, IRMA, haemorrhages and venous beading.

Cotton wool spots: White patches with fraying borders merging into the retina, present in areas of microvascular occlusion and nonperfusion.

IRMA: Intra retinal vascular shunts and they do not leak on fluorescein angiography.

II. MACULOPATHY

It is one of the major causes of visual loss in diabetic retinopathy. It is more commonly associated with NIDDM and older patients. Maculopathy presents either as macular edema ormacular ischaemia. Macular edema can present as focal or diffuse edema which may be clinically significant.

Focal macular edema:

- **areas of leakage from micro aneurysm and IRMA.**
- **associated with rings of hard exudates and microaneurysms**

Diffuse macular edema:

- **has diffuse retinal thickening**
- **wide spread retinal capillary abnormality with diffuse leakage due to extensive breakdown of blood retinal barrier.**
- **associated often with cystoid macular edema.**

Macular Ischaemia: capillary nonperfusion

- microaneurysm clusters at the margins of nonperfusion

- more visual loss with clinically normal appearing macula
- enlargement of foveal avascular zone
- if >1000 micron in diameter, severe visual loss ensues.

Clinically significant macular edema (CSME):

The CSME was defined by ETDRS which helps in its management. 10% of diabetics have macular edema and in 40% of these, the center of the macular is involved and have significant visual loss.

III. Proliferative Diabetic Retinopathy (PDR)

The appearance of new vessels over disc or elsewhere in the retina is considered as PDR. The most plausible explanation for endothelial proliferation is ischaemia of inner retinal layers secondary to closure of parts of retinal capillary bed. Based on the location the new vessels can be grouped as

- New vessels involving the retina but sparing the disc
- New vessels involving the disc
- New vessels in the anterior chamber angle

STAGES OF PDR

Stage of proliferation

- Fine new vessels at the disc margin of size one eighth to one fourth that of major retinal vein.
- New vessels more frequently occur along supero-temporal vein and grow along retinal plane or invade vitreous either radially or irregularly.
- Deposition of fibrous tissue around blood vessels.

Stage of regression

Decrease in the calibre and the number of vessels occurs and it is followed by replacement of them with fibrous tissue.

SEQUELAE

1. Contraction of vitreous

- Thickened posterior vitreous adjacent to the site of new vessels with fibrous tissue along its posterior surface.
- Vitreous contraction with the vector pulling the posterior vitreous forward.
- Eventual posterior vitreous detachment commonly occurs along superotemporal vessels, temporal to macula and above/ below the disc. The traction on new vessels can lead to vitreous haemorrhage.

2. Tractional retinal detachment

The occurrence and severity of retinal detachment is influenced by the timing and degree of vitreous shrinkage and vitreoretinal adhesions. With contraction of fibrovascular proliferation, distortion and displacement of macula occurs. Macula is usually dragged nasally and vertically.

3. Involutional diabetic retinopathy

With complete vitreous contraction and detachment, marked reduction in the calibre of retinal vessels is characteristic. There is severe retinal ischaemia, resulting in marked visual **loss.**

Clinical Evaluation

Visual Acuity

The evaluation of retinopathy patients starts with assessing visual acuity. Refraction is to be done in all cases of diabetic retinopathy and best corrected visual acuity must be documented.

Colour vision

In diabetes, the sensitivity of blue cones is depressed and the common defect observed is in the blue-yellow range. It is best detected by fransworthmunsell hundred hue test.

Fields

Examination of fields by perimetry shows areas of scotoma which represent the corresponding abnormal areas of retina.

Intraocular pressure

IOP is measured in diabetics to rule out secondary glaucoma.

Ophthalmoscopy

By direct ophthalmoscopy, detailed fundus examination is carried out. Even though the area visualized is smaller, it provides a good magnification for the details to be seen clearly. Indirect Ophthalmoscopy is carried out to visualize the entire retina including peripheral retina.

Slit Lamp Examination

Using slit lamp biomicroscope, the retinal examination and angle study are done with Goldmann 3 mirror lens, +78D and 90D lens.

Macular Function Tests

The assessment of macula is recommended in all cases of maculopathy. The following tests can be performed:

1. 2 point discrimination
2. Photo stress Test
3. Amsler grid test
4. Blue field entoptoscope

Flourescein angiography indications in diabetic retinopathy:

- to define the focal and diffuse leaks in diabetic maculopathy
- to delineate the extent of ischaemic zone in maculopathy
- to locate areas of capillary nonperfusion and leakage from new vessels in proliferative stage

- to identify the persistence, progression or resolution of macular edema following laser photocoagulation.
- to detect small microaneurysms <20 microns

The property of fluorescein to absorb higher energy, shorter wavelength blue light and to emit lesser energy, longer wavelength, green light, with this change occurring over a brief period of time (<10-8) is called fluorescence. This property is used in fluorescein angiography

Features

Microaneurysms: well-definedhyperfluorescence against dark choroidal background Retinal haemorrhages: well defined areas of hypoflourscence.

- Superficial: blocked retinal & choroidal fluorescence.
- Deep: blocked choroidal fluorescence alone Hard exudates: areas of blocked fluorescence Cotton wool spots: areas of blocked fluorescence.

Capillary nonperfusion: well defined areas of hypoflourescence between retinal vessels. Non visibility of capillaries

NVD/NVE: increasing intense hyperfluorescence due to leakage.

Focal macular edema: focal leaks from microaneurysms with blocked fluorescence from hard exudates and haemorrhages.

Diffuse macular edema: dilatation of capillaries and diffuse leaks in early venous phase. Floral pattern in cystoid macular odema.

Ischaemic maculopathy: enlarged and irregular foveal avascular zone , capillary dropouts in perifoveal area.

Management

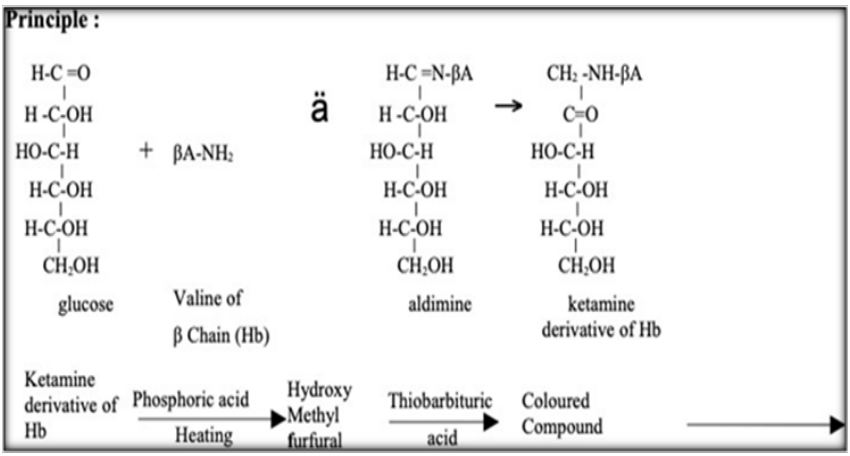
Evaluation biochemical parameters

1. Estimation of Fasting Blood Glucose

This is done by orthotoludine method.

2. Glycosylated heamoglobin (HbA1c)

Estimation of HbA1c is done using high pressure liquid chromatography.



This coloured compound is then measured.

3. Total Cholesterol (Modified Salkowski's Method– Wybenga Method)

The principle of this reaction is that cholesterol reacts with ferric chloride ions in acetic acid followed by sulphuric acid. This method is modified by Wybenga and this is used to estimate total cholesterol.

4. HDL Cholesterol (Loper and Virella)

In this procedure, the VLDL, chylomicrons and LDL are separated by phosphotungstate in the presence of Mg+ ions and HDL cholesterol is estimated from the supernatant.

5. Triglycerides (Foster and Dunn) Hantzsch Reaction

Triglycerides are extracted by heptane isopropanol from phospholipids and are saponified by potassium hydroxide.

The liberated glycerol is oxidised to formaldehyde which then combines with acetyl acetone and ammonia to give a dihydrobutidine derivative. It is then measured.

Treatment

The treatment depends on the type and severity of retinopathy.

Non-proliferative retinopathy

For mild and moderate NPDR, strict adherence to normal levels of glycemia, blood pressure and lipid status is the mainstay of the treatment. Scatter laser photocoagulation is generally not recommended.

The Early Treatment Diabetic Retinopathy Study and the Diabetic Retinopathy Study recommend photocoagulation as the treatment of choice for severe and progressive form of retinopathy and clinically significant macular edema.

Severe NPDR

For severe NPDR, scatter laser treatment is appropriate when disease process is progressing rapidly.

Close follow-up unlikely.

Macular edema

ETDRS demonstrated that retinal laser therapy applied to macula reduces the risk of substantial worsening of vision by 50%.

a) Focal macular edema:

Direct laser using green or yellow wavelength applied over microaneurysms that are between 500-3000µm from the center of the macula. Parameters for focal treatment are:

Spot size: 50-100µm

Duration: ≤0.1s

Power: sufficient to cause blanching of microaneurysm / RPE

b) Diffuse macular edema:

A light intensity grid pattern using green or yellow wavelength to all areas of diffuse leakage

>500µm from the centre of macula and 500µm from the temporal margin of the optic disc. Parameters for grid pattern.

Spot size: 50-100µm Duration: ≤0.1s

Power: sufficient to cause blanching of RPE

Spots are placed at least one burn width apart. CSME is more benefited from laser.

c) Ischaemic maculopathy:

As the macula has capillary non perfusion, focal or grid laser is not recommended.

Image: showing Grid laser done on a patient.

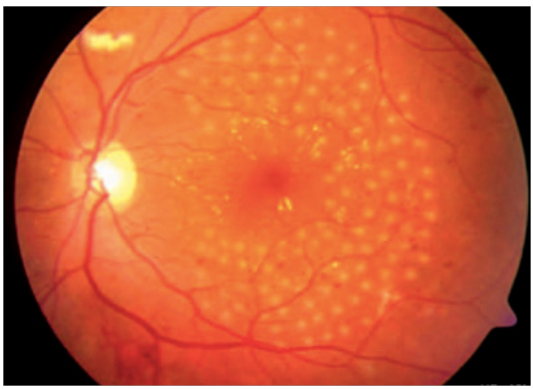
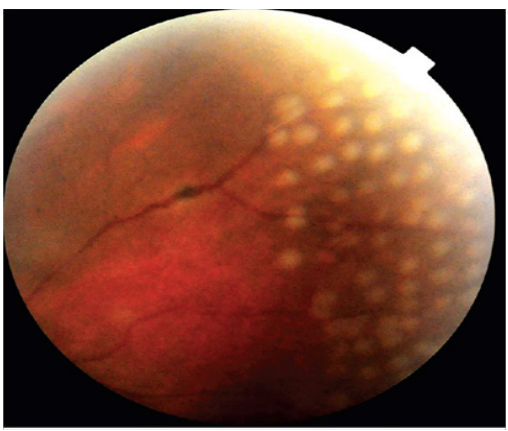


Image: showing Sectoral laser done on a patient



Proliferative Diabetic Retinopathy

Medical management:

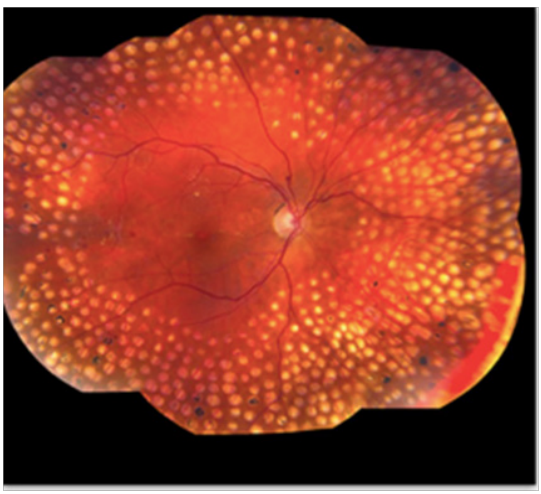
The principal goal is controlling both systemic and local factors that influence the progression from NPDR to PDR. This includes good glycemic control, control of hypertension, renal disease and coronary artery disease.

DCCT and UKPDS have documented that intensive glycemic control is associated with a reduced risk of newly diagnosed retinopathy and a reduced progression of existing retinopathy.

Panretinal photocoagulation (PRP):

PRP is done to cause regression of existing new vessels to prevent progressive neovascularisation.

Image: Showing pan retinal photocoagulation done in a patient having diabetic retinopathy



ETDRS and DRS study model, the parameters are Number of burns: ≥1200

Spot size: 500µm

Duration: 0.1.

Spots are placed at least 1⁄2 burn width apart and the number of sessions are more than two. The rate of severe visual loss is reduced from 16% in untreated eyes over two years to 6% in treated eyes, documenting a reduction of 57%.

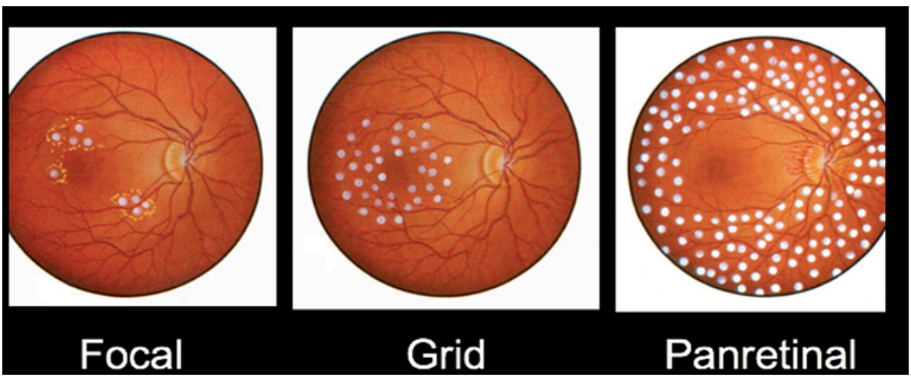
Surgical management

The mainstay of contemporary management for vitreous haemorrhage and tractional retinal detachment is surgery.

Indications for pars plana vitrectomy:

- Dense non clearing vitreous haemorrhage
- Tractional retinal detachment threatening macula
- Combined tractional and reghmatogenous detachment
- Diffuse macular edema with post hyaloid traction
- Recurrent vitreous haemorrhage

Image: Showing different lasers done for diabetic retinopathy



Recent Advances

In patients with refractory CSME, intravitreal administration of corticosteroids or anti VEGFS has proven to be useful. Currently, several drug delivery modalities are in clinical trials to investigate their efficacy.

ETDRS Recommended Ocular Examination Schedule

Age at Onset	Time Recommended	Routine Minimal
≤ 30 yearly	5 years of diabetes	yearly
> 30 yearly	At the time of diagnosis	yearly
Pregnancy	Before conception/ first trimester	3 monthly

Recommended Follow-up Schedule in Diabetic Retinopathy Patients

Dr Erum KhateebRetinal Abnormality	**Suggested Followup**
Normal or rare micro aneurysms	Annually
Mild NPDR	Every 9 months
Moderate NPDR	Every 6 months
Severe NPDR	Every 4 months
CSME	Every 2-4 months
PDR	Every 2-3 months

Levels of Prveventionof Diabetic Retinopathy

The visual loss due to diabetes can be prevented by doing intervention at various stages of the disease.

Primary prevention

Once the diagnosis of diabetes is made, strict control of glycemic status by diet, exercise and drugs should be done.Periodic ophthalmic examination must be carried out. Referral of the diabetic individuals to ophthalmologists regularly or as soon as signs of micro angiopathy like microalbuminuria sets in should be done.

Secondary prevention

In NPDR patients by the modification of the risk factors blindness can be prevented. Fundus fluorescein angiography is

done to find out the type of maculopathy at initial stages. Laser photocoagulation is done for maculopathy and PDR to prevent visual loss.

Tertiary prevention

When the patient is in advanced proliferative stage, relevant surgical treatment is given. Further visual rehabilitation is given by low vision aids.

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