# Diabetic Retinopathy-The Indian Scene

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Diabetic retinopathy, is today the major cause of blindness in the industrialised western world. In India, it was the 17th cause of blindness a couple of decades ago but to-day diabetes related blindness has rapidly ascended to the sixth position[1].

Diabetic retinopathy often does not manifest itself with loss of vision until it is almost too late to intervene. The risk of developing diabetic retinopathy is higher for patients who have had diabetes for a long time and with poor glycaemic control. Luckily however, not all patients who have diabetic eye changes have sight threatening forms of retinopathy and only a few patients ultimately become blind due to diabetes.

Diabetic retinopathy (DR) if not treated at an early stage invariably progresses to irreversible blindness. However laser treatment given at an early stage is effective in maintaining or improving the visual acuity in upto 60% of cases.

### Aetiology and Prevalence

Diabetes Mellitus is present in 4-5% of the population in India compared to 1-2% percent in UK and other European countries. At our centre the overall prevalence of diabetic retinopathy in Non-Insulin Dependent Diabetics is 33.7%.[2] After twenty years of diabetes, we found that 70% of our diabetics had some form of diabetic retinopathy and about 10% had proliferative diabetic retinopathy (PDR).

### Classification and Clinical Features

As high risk lesions responsible for blindness in diabetes are often asymptomatic it is therefore imperative that doctors responsible for the care of diabetics should be familiar with the ophthalmoscopic features of diabetic retinopathy. Various grading systems of retinopathy have been in use, but the Hammersmith Hospital grading system[3] has been used at our centre to grade the lesions of diabetic retinopathy as it is simple and very useful clinically.

Diabetic retinopathy can be basically classified into two major types:

I. Non-Proliferative or Background Diabetic Retinopathy or

II. Proliferative or Advanced Retinopathy

**i. Non-Proliferative Retinopathy:** This can be further subdivided into:

a. Non-Proliferative Retinopathy without Macular Involvement which includes microaneurysms, haemorrhages and/or hard exudates within the major temporal vascular arcades or elsewhere on the retina.

b. Non-Proliferative Retinopathy with Macular Involment or (Maculopathy) includes haemorrhages and/or hard exudates within one disc diameter of the macula, with or without visual loss. Maculopathy can be of two forms:

i) Exudative Maculopathy when oedema, haemorrhages and/or hard exudates develop in the macula.

ii) Ischaemic Maculopathy indicates widespread capillary closure affecting the macula.

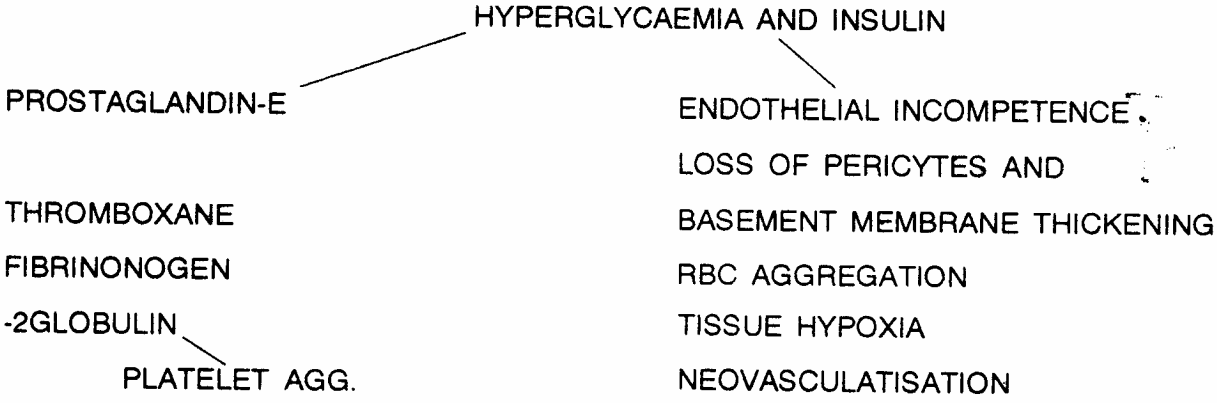
c. Pre-Proliferative Retinopathy is an intermediatary stage characterised by venous irregularities (beading, loops and reduplication) and/or multiple haemorrhages and/or multiple cotton wool spots and/or intra retinal microvascular abnormalities (IRMA) and extensive capillary dropouts.

This stage indicates widespread retinal ischaemia and hence the possibility of progression to new vessel formation on the retina within a short period of time (usually within two years).

II. **Proliferative Diabetic Retinopathy** new vessels on the optic disc and elsewhere on the retina, pre-retinal haemorrhages and fibrosis on the surface of the retina.

The new vessels grow into the vitreous. They are very friable and bleed producing a vitreous haemor-

**Fig 1-Pathogenesis of Diabetic Retinopathy**



rhage, and this leads to fibrous proliferation with eventual retinal detachment. The new vessels are often asymptomatic until they breakdown and bleed, when the patient complains of seeing dark "floaters" in the field of vision. A frequent complication of proliferative retinopathy is rubeosis iridis, in which blood vessels appear on the surface of the iris and obstruct the drainage angle of the eye, precipitating neovascular glaucoma.

Hence the two sight threatening stages of diabetic retinopathy requiring immediate treatment are Maculopathy and Proliferative Diabetic Retinopathy.

### Pathogenesis

The pathogenesis and pathological findings in diabetic retinopathy are outlined in Figure 1. The two main features are:

1. Breakdown of the blood retinal barrier and loss of pericytes between the endothelial cells of the retinal capillaries. This results in out-pouching of the capillary wall, (micro-aneurysms) leakage of fluid, (retinal odema) leakage of blood (haemorrhages) and exudation of macrophages with lipids (hard exudates).
2. Microvascular ischaemia resulting in the formation of new vessels on the disc and on the surface of the retina. These vessels being friable bleed into the vitreous or on to the retina (Proliferative Retinopathy).

### Screening for Diabetic Retinopathy

It is only with the combined effort of diabetologists and ophthalmolgists that implementation of a screening programme for diabetic retinopathy is possible in our country. Efficient, objective methods are available to detect high risk lesions and blindness can be prevented if appropriate laser treatment is instituted early.

### Who should do the Screening?

Ideally, screening for diabetic retinal disease should be done by an ophthalmolgist trained for this purpose. When this is not feasible, screening should be the primary responsibility of the doctor in charge of the diabetic patient. This has been endorsed by the 1990 convention on Diabetic Retinopathy by diabetologists and ophthalmologists of Europe.

### When to Screen?

It is mandatory that every patient should have a fundus examination at the time of diagnosis of diabetes. This is because, in NIDDM patients diabetic retinopathy could be present even at the time of diagnosis of diabetes, due to the insidious nature of this disease and the long asymptomatic period.

In a study where we screened 1563 newly detected diabetics (i.e. with a duration less than 1 year of diabetes) we found that 120 patients i.e. 5.7%. had diabetic retinopathy at the time of diagnosis of diabetes! In a break-up analysis we, found that 90 patients had early Non-Proliferative diabetic retinopathy, 28 had moderate to severe Non-proliferative diabetic retinopathy and 2 patients even had Proliferative diabetic retinopathy (PDR) at the time of diagnosis of diabetes Similar findings have also been documented by Klein et al in their studies[4].

If the retina is normal, the follow-up examination should be done on an annual basis, but more frequently if lesions of diabetic retinopathy are already present.

In IDDM patients the retina should be first examined at the time of puberty or within five years after the diagnosis of diabetes whichever is earlier and annually thereafter. If diabetic retinopathy is complicated by an intercurrent illness or renal disease, more frequent examinations should be done.

The fundi should also be examined if patients complain of visual symptoms such as impaired central vision, distorted vision or seeing black floaters which may be caused by a vitreous haemorrhage.

### How to Screen?

It is essential that all diabetic patients should be screened on a regular basis for retinopathy and other ocular disorders. Visual acuity should be recorded each time the patient has an eye examination, although testing for visual acuity is not, by itself, a suitable substitute for ophthalmoscopy. Screening should be carried out by someone fully competent in the use of an ophthalmoscope, and in the recognition of fundus abnormalities. If visual acuity is worse than 6/6, the refractive error should be corrected using the patient's spectacles for distant vision.

The pin hole test can be used to differentiate between impaired vision due to refractive error and that due to pathology in the eye. The patient views the test chart through a pin hole held close to the eye, which overcomes refractive error and improves vision. If use of the pin hole causes the vision to worsen, it may be indicative of an abnormality, such as macular oedema or cataract.

The ocular adenxa and the anterior segment should be examined by a biomicroscope (slit lamp) to rule out other causes of visual loss. The intra ocular pressure and the angles of the eye should be checked.

After adequate dilatation of the pupils, a detailed examination and documentation of the lesions of diabetic retinopathy should be done by ophthalmoscopy. Both direct and indirect ophthalmoscopy should be done for a comprehensive assessment of the retinal lesions.

Non-mydriatic cameras can be used for documentation[5] but their resolution for new vessels is limited and hence detection of fine new vessels may be difficult. Peripheral lesions may also be overlooked.

Fundus fluorescein angiography (FFA) is a necessary prelude to monitor patients who require laser therapy. In cases of early macular odema causing visual loss which may not be easily detected by opthalmoscopy, FFA should be done to document the oedema. FFA is also useful in identifying neovascularisation, delineating areas of retinal capillary nonperfusion and in monitoring regression of neovascularisation after laser therapy. In certain cases, FFA is also useful in detecting revascularisation and perfusion of ischaemic areas after laser therapy has been done[6]. This procedure involves the injection of a bolus of fluorescein (dye) into the anterior cubital vein and rapidly taking pictures of the central and peripheral retina.

Vitreous fluorophotometry is a technique which is used to detect the early breakdown of the blood retinal barrier. Being a laborious procedure, it remains as a research tool to-day.

## Treatment

**Laser Photocoagulation** has been the single greatest hope of the century for patients with diabetic retinopathy. Several multicentric studies all over the world conclusively demonstrated that laser photocoagulation prevents blindness due to diabetes. The exact mode of action of the lasers is still not completely understood.

The Diabetic Retinopathy Study (DRS) demonstrates unequivocally the treatment benefits of pan retinal photocoagulation (PRP) of proliferative diabetic retinopathy[7] This treatment helps to reduce severe visual loss from vitreous haemorrhage.

### New vessels on the disc

Scatter laser photocoagulation or panretinal photocoagulation is delivered in these cases. The laser burns are mainly concentrated in the extreme periphery and midperiphery of the retina. Thus the hypoxic areas, which seem to be one of the vaso stimulating factors leading to the development of new vessels, are completely converted into anoxic areas. This results in the regression of the new vessels. In cases where new vessels are persistent on the disc further "fill in" PRP treatment is necessary.

### New-Vessels elsewhere on the retina

For new vessels elsewhere on the retina a pan retinal photocoagulation (PRP) should be done. If focal treatment of the segment with new vessels is done, close monitoring should be done for detecting subsequent neovascularisation of the other areas of the retina. Data from the Diabetic Retinopathy Study (DRS) showed that focal treatment of new vessels on the disc or elevated new vessels elsewhere on the retina did not achieve better results than scatter photocoagulation (PRP).

### New Vessels with associated fibrosis

Pan retinal photocoagulation should be done discretely, avoiding the fibrous tissue especially in areas of traction. Vitrectomy is indicated if traction retinal detachment extends to include the macula.

### Vitreous Haemorrhage

In patients where the vitreous haemorrhage is not very dense and parts of the retina are visible by a direct ophthalmoscopic examination, laser treatment should be tried. The peripheral ischaemic retina should be treated as far as possible. Non-resolving dense vitreous haemorrhage should be referred for vitrectomy[8] especially if known traction

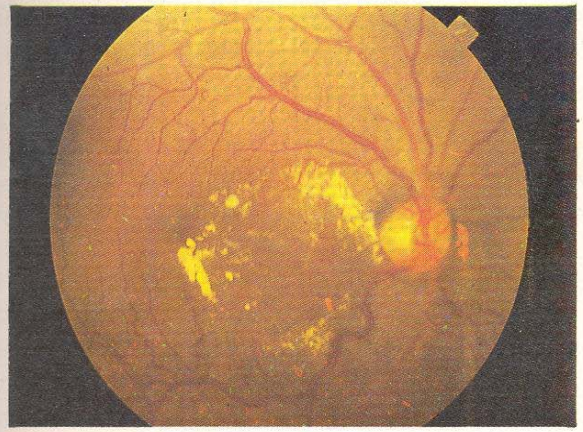
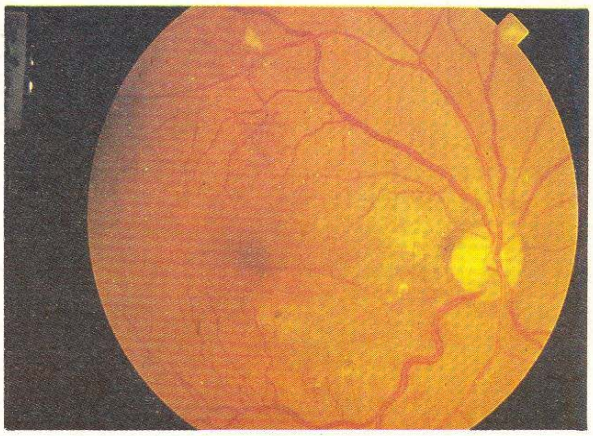


Fig-2 - 2a Colour Photograph of Exudative Maculopathy



2b One year after Laser Therapy

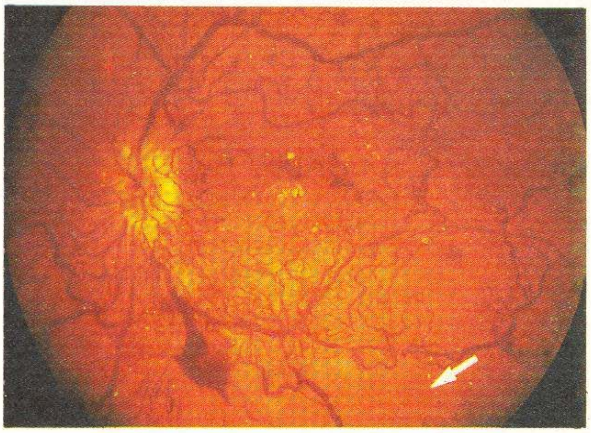


Fig-3 Proliferations on the disc extending on to the Retina

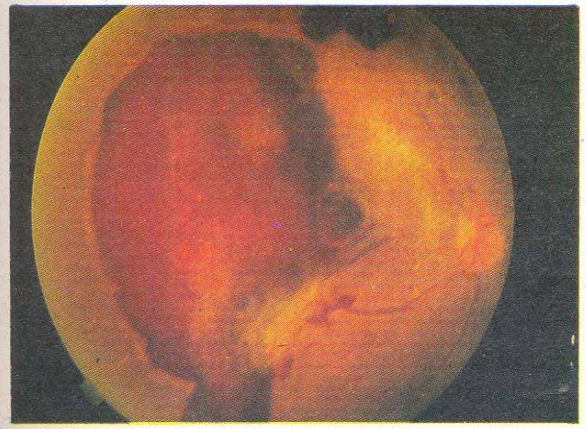


Fig-4 Retinal Haemorrhage in the Macula

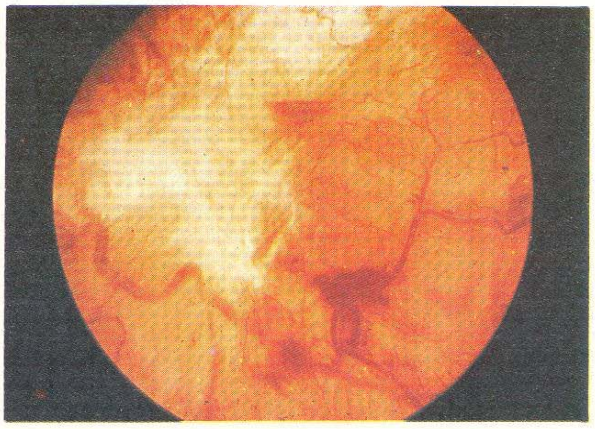


Fig-5 Retinitis Proliferans with Traction Retinal Detachment

macular detachment, treatable maculopathy or rubeosis iridis exists.

### Diabetic Maculopathy

The value of focal photocoagulation for diabetic macular odema was assessed by the Early Treatment Diabetic Retinopathy study[9] (ETDRS). This study clearly showed that in carefully selected cases, laser treatment substantially lowered the risk of visual loss. Focal laser treatment may be done in cases with circinate rings or microaneurysms close to the fovea. The use of the argon green, yellow or red lasers is recommended as the argon blue is absorbed more by the luteal pigment in the macula leading to nerve fibre damage.

In cases of widespread macular oedema, a grid pattern of laser treatment is recommended. If applied before the oedema damages the nerve fibre layer, remarkable improvement of visual acuity can be noted. The end point of successful treatment is reversal of oedema, FFA is needed to detect focal leakage and to monitor the effect of laser treatment.

In a study done in our centre, we screened 15,200 consecutive NIDDM patients and 3,700 eyes had laser requiring retinopathy. Of these 3100 eyes underwent focal treatment for maculopathy and 600 eyes had PRP for Proliferative Diabetic Retinopathy[10].

### Retinopathy in Secondary Forms of Diabetes

It was hitherto believed that retinopathy is rarely seen in the secondary forms of diabetes as in Fibrocalculous Pancreatic Diabetes (FCPD), Pancreatic carcinoma, Pancreatectomy etc. In a study[11] done at our centre it has been documented that diabetic retinopathy occurs in FCPD with the same prevalence rate as in NIDDM. Severe forms of retinopathy like maculopathy and proliferative diabetic retinopathy also do manifest in FCPD of long duration. Thus this shows that retinopathy can occur in all forms of diabetes if prolonged and severe hyperglycaemia is present.

### Do Genetic Factors Influence Retinopathy?

It has been clinically documented that sometimes long term diabetics with severe hyperglycaemia do not develop any retinopathy even after twenty to thirty years duration of diabetes. This led to the design of a study in which we recently looked at the genetic susceptibility of diabetic retinopathy. This data suggests that there is a genetic association with proliferative retinopathy in NIDDM of South Indian origin. It was shown that switch region of IgA heavy chain (S1) gene is associated with protection from proliferative diabetic retinopathy in South Indian NIDDM diabetics[12].

### Future Research in Diabetic Retinopathy

The Sorbinil Retinopathy trial[13] was initiated in 1983 to determine whether sorbinil (aldose reductase inhibitor) could delay the onset or slow the progression of diabetic retinopathy. The demonstration of polyol pathway activity in the pericytes of the retinal capillaries being affected early in the development of diabetic retinopathy, led to the design of this study. But it was shown that sorbinil did not have a clinically important effect on retinopathy in IDDM of moderate duration.

Researchers in eye disease are opening up a new avenue of study to prevent or reverse proliferative diabetic retinopathy by using alpha interferon. This is a naturally occuring substance, and part of the body's immune system. Alpha interferon appears to inhibit or slow down the growth of new blood vessels. Miller and associates showed that alpha interferon brought about regression of new vessels on the irises of monkeys. But clinical trials in humans have yet to be done to prove the efficiency and safety of this drug.

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