Our Patient has Diabetes: Will it Affect his Retina?
(Diabetic Retinopathy)

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Introduction

Diabetic retinopathy (DR) is defined as the progressive dysfunction of the retinal vasculature due to chronic hyperglycaemia resulting in structural damage to the neural retina.[1]

The prevalence of diabetic retinopathy varies substantially between studies, even among contemporary populations in the same country but is estimated to be around 21.7% on a pan India scale according to a cross-sectional study conducted by the All India Ophthalmologists' Society (AIOS) in 2014.[2] It is more common in type I diabetes than in type II, and sight-threatening disease is prevalent in 10% of patients. Proliferative diabetic retinopathy affects 5-10% of the diabetic population; type I diabetics are at particular risk, with an incidence of up to 90% after 30 years.[3]

Risk factors for diabetic retinopathy include duration of diabetes, poor control of blood glucose, pregnancy, hypertension, nephropathy, hyperlipidaemia, smoking, obesity and anaemia. Out of these, duration of diabetes constitutes the most important risk factor; incidence of DR is 50% after 10 years and 90% after 30 years.[3]

DR is predominantly a microangiopathy but direct hyperglycaemic effects on the blood vessels are also likely to play a vital role. Vascular endothelial growth factor (VEGF) is one of the most commonly implicated factors in the pathogenesis of DR.[1]

According to Early Treatment Diabetic Retinopathy Study (ETDRS), DR is classified, predominantly, into the following categories:[3]

- Non-proliferative Diabetic Retinopathy (NPDR)
- Proliferative Diabetic Retinopathy (PDR)
- Diabetic Maculopathy

Symptoms of DR are painless, gradual and progressive diminution of vision, floaters, frequent change in refractive errors and complete loss of vision.

Clinical signs of DR include

- Microaneurysms which are localised outpouchings of the capillary wall due to loss of pericytes
- Retinal haemorrhages
- Hard exudates
- Macular oedema, which is more common in type II diabetes than in type I diabetes
- Cotton wool spots which are soft

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exudates formed due to infarcts in the nerve fibre layer of the retina

- Venous changes like looping, beading, generalised dilatation and tortuosity
- Intraretinal microvascular anomalies (IRMA)
- Arterial changes like peripheral narrowing and obliteration
- New vessels at the optic nerve head, new vessels elsewhere in the retina, new vessels on the iris.

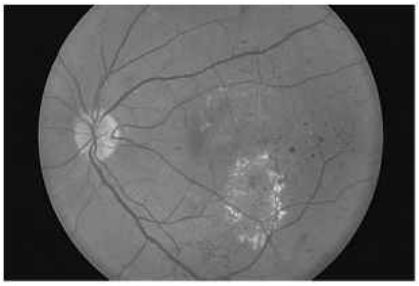

Fig. 1.1 : Non-proliferative DR showing microaneurysms and dot blot haemorrhage with hard exudates[3]

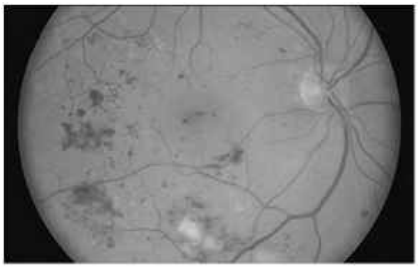

Fig. 1.2 : Non-proliferative DR showing dot blot haemorrhages, cotton-wool spots[3]

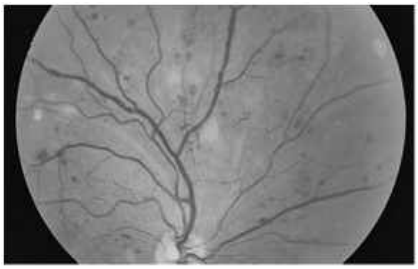

Fig. 1.3 : Severe NPDR with microvascular anomalies and venous beading[3]

Diagnosis of DR is mainly clinical and can be easily made in the clinic with an indirect ophthalmoscope, direct ophthalmoscope, and slit-lamp bio-microscopy. Other modalities which can prove extremely fruitful in the diagnosis of DR are fundus-fluorescein angiography.

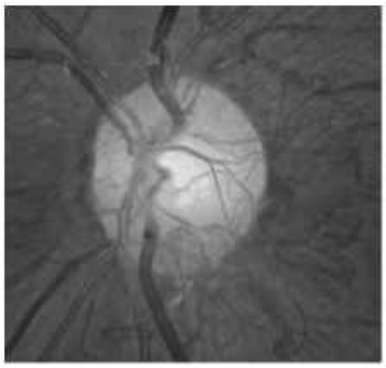

Fig. 1.4 : New vessels at Optic disc[3]

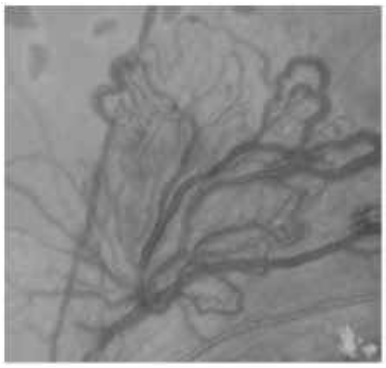

Fig. 1.5 : New vessels elsewhere[3]

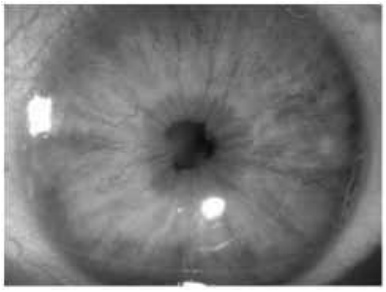

Fig. 1.6 : New vessels on iris[3]

(FFA) and Optical Coherence Tomography (OCT). The latter is

particularly useful in providing information regarding macular oedema and its extent and the overall thickness of the macula. Ancillary testing is indispensable for documentation and monitoring of the disease process.

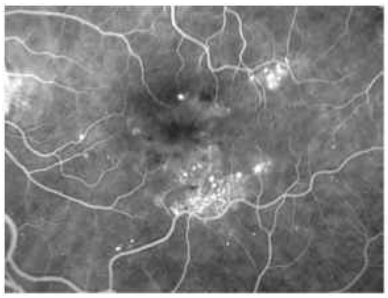

Fig. 1.7 : FFA shows leaking microaneurysms and central diffuse hyperfluorescence with a flower-petal configuration[3]

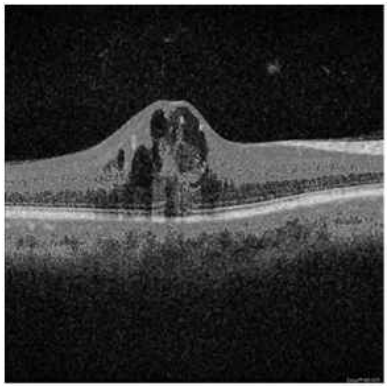

Fig. 1.8 : OCT showing retinal thickening and cystoid spaces in the macula[3]

In the era of Artificial Intelligence (AI), it would be worthwhile mentioning its use in the screening of DR Cystoid Macular Oedema (CME). Researchers in the Google Brain initiative have developed a self-optimising algorithm that can examine large numbers of fundus photographs and can automatically detect diabetic retinopathy and diabetic macular oedema with an incredibly high degree of accuracy. In order to test the algorithm's performance, a research was carried out on two groups of images (N=11, 711), and it was found to have a sensitivity of 96.1% and 97.5%, and a specificity of 93.9% for DR and CME, respectively. Although, AI has remarkable scope in the management of DR in the coming years, it will be prudent to highlight that it can never replace a skilled clinician and his intelligence.[4]

Patient education and counselling play a pivotal role in the management of DR. Strict glycaemic control should be adhered to along with cessation of smoking and other lifestyle modifications.

The Diabetes Control and Complication Trial (DCCT) was designed to evaluate whether Intensive Treatment (INT), with the goal of achieving blood glucose levels to as close to the non-diabetic values as possible, reduced the onset and progression of microvascular complications accompanying the disease process of Type I diabetes compared with the Conventional therapy (CON). DCCT conclusively demonstrated that intensive control of blood glucose levels significantly reduced risk of microvascular complications in patients with Type I Diabetes.[5]

Whereas DCCT revolved around intensive treatment and microvascular complications in Type I Diabetes, The UK Prospective Diabetes Study (UKPDS) was conceived to dictate newer guidelines for management of Type II Diabetes, as these patients commonly have other risk factors like obesity, hypertension and hyperlipidaemia. The design of UKPDS trial is given in Fig. 1.9.[6]

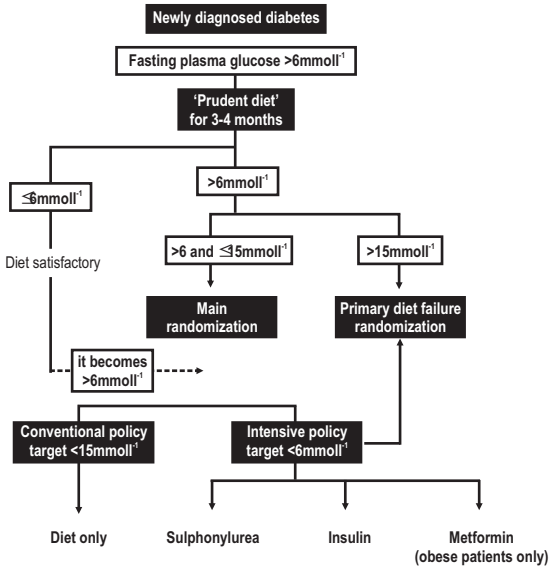

Fig. 1.9 : Design of UKPDS[6]

Diabetic patients, even if asymptomatic and with good glycaemic control, must be motivated to undergo an annual ophthalmic examination to detect early changes of diabetic retinopathy. Recommendations regarding follow up visits as per the Early Treatment Diabetic Retinopathy Study (ETDRS) classification are given in Table 1.1.

Category	Follow-up
No DR	Review in 12 months
Very mild NPDR	Review in 12 months
Mild NPDR	Review within 6-12 months
Moderate NPDR	Review in 6 months
Severe NPDR	Review in 4 months
Mild-to-moderate PDR	Treat as soon as detected. If not treated, review in 2 months
High risk PDR	Treat immediately

Table 1.1 Follow up in the management of DR[3]

Early stages of DR can be observed. Treatment options in the management of severe and advanced DR are intravitreal anti-VEGF agents like ranibizumab (Lucentis) or bevacizumab (Avastin), intravitreal triamcinolone, LASER photocoagulation, micro-pulse diode LASER, and pars plana vitrectomy.

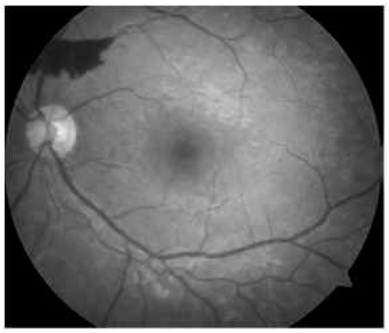

Fig. 1.10 : Limited pan-retinal photocoagulation[3]

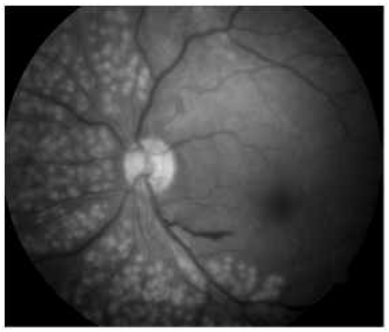

Fig. 1.11 : Extensive pan-retinal photocoagulation[3]

Ranibizumab (Lucentis) is the first FDA-approved anti-VEGF agent for the treatment of diabetic retinopathy with or without diabetic macular oedema. A study conducted on the review of Ranibizumab in the treatment of diabetic macular oedema has shown that Ranibizumab improves visual acuity and reduces the central macular thickness in diabetic maculopathy. It is the first-line therapy for diabetic macular oedema. Although Pan-retinal Photocoagulation is the first-line treatment for PDR, emerging data show that it may be used in the management of

PDR, and has an excellent safety profile, with lower incidence of ocular and systemic side The ETDRS has shown that Argon LASER photocoagulation reduces the risk of severe visual loss due to DR, and recommends focal LASER to individual leaking microaneurysms, and grid LASER to diffuse leakage and capillary non-perfusion. Modified ETDRS recommends direct LASER treatment to all leaking microaneurysms between 500 and 3000 microns from the macular centre but not within 500 microns of the optic disc. The recommended burn spot size of 50 microns and duration is 0.05 to 1 sec.[8] LASER treatment essentially reduces the ischaemic retinal load by selectively targeting retinal cells in the hypoperfused areas, decreasing relative ischaemia, thus reducing production of angiogenic factors and improving oxygenation of vitreous. The most devastating complications of DR are grouped under the category, 'advanced diabetic eye disease' which includes sub-hyaloid haemorrhage, vitreous haemorrhage, and tractional retinal detachment. These are indications for management via the surgical approach, that is, pars plana vitrectomy. In recent times, Micro-Incision Vitrectomy Surgery (MIVS) has gained popularity. MIVS is a sutureless procedure and offers greater patient comfort; lesser surgically induced refractive error, lesser conjunctival scarring and faster rehabilitation. Port design allows more complete vitrectomy and easier dissection of proliferative membranes. Higher cut rates and smaller port aperture offer the advantage of preclusion of inadvertent iatrogenic retinal breaks.[9] Sub-hyaloid haemorrhage, apart from vitrectomy, can also be subjected to lysis by Neodymium: Yttrium Aluminum Garnet (Nd: YAG) laser.

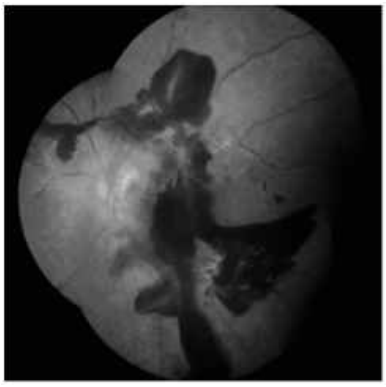

Fig. 1.12 : Advanced diabetic eye disease with vitreous haemorrhage[3]

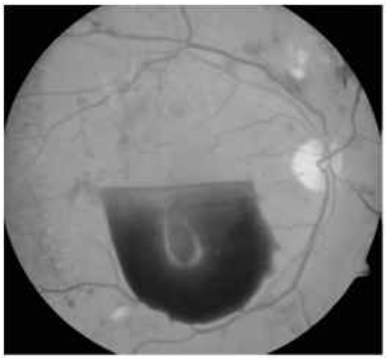

Fig. 1.13 : Advanced diabetic eye disease with sub-hyaloid haemorrhage[3]

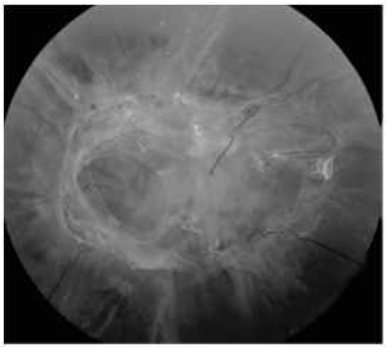

Fig. 1.14 : Advanced diabetic eye disease with tractional retinal detachment[3]

GUIDELINES FOR REVIEW AND REFERRAL TO AN OPHTHALMOLOGIST ARE AS FOLLOWS[10]

1. *Review but referral is not appropriate*

a. Normal fundus

b. Mild non proliferative diabetic retinopathy with small haemorrhages and/or small hard exudes more than one-disc diameter from fovea.

2. *Routine referral to ophthalmologist*

a. NPDR with large exudates within the major temporal arcades but not threatening the fovea

b. NPDR without maculopathy but with reduced visual acuity to determine causes of visual impairment

3. *Early referral to ophthalmologist*

a. Clinically Significant Macular Oedema (CSMO)

b. Pre-proliferative DR

4. *Urgent referral to ophthalmologist*

a. Proliferative DR

b. Pre-retinal or vitreous haemorrhage

c. Rubeosis iridis

d. Retinal detachment

Take Home Message

Diabetic retinopathy is a sight threatening complication of diabetes mellitus which can raise the magnitude of the morbidity associated with the disease, significantly. It can lead to considerable physical and psychological impacts on the patient arising from the visual impairment, and disturbance in the daily activities of the patient, thus, curbing the patient's independence to a pronounced level. It is, therefore, of paramount importance, that this complication of diabetes be detected and treated at the earliest to preserve vision to as great an extent as would be possible at the stage of DR at which it is detected. Patient education and counselling, undoubtedly, are indispensable in the management of DR. The practitioner must be cognisant that stringent, regular follow up forms the core of management of DR and its complications, and the patient must be made aware of the gravity of this complication of diabetes and the need for strict glycaemic control and lifestyle modifications alongside of the regular follow up visits.

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