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Symposium On Diabetes

Diabetic Retinopathy

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Introduction

Chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels¹.

Specific to diabetes, and occurring in both type 1 and type 2 are the various diabetic microvascular complications. Characterized by involvement of vascular cells of capillaries, arterioles, and basement membrane, they affect the retina the kidney and the nerves.

Defined as ***“Progressive dysfunction of the retinal vasculature caused by chronic hyperglycemia”***, diabetic retinopathy remains the number one cause of new blindness even in most industrialized countries².

Diabetes mellitus causes damage to the retinal vascular endothelium leading to retinal vascular leakage and neovascularization. Visual loss results from complications such as diabetic macular edema, vitreous hemorrhage, and retinal detachment.

“Blindness” is defined as the inability to perform any task for which vision is essential. The term ***“partially sighted”*** indicates substantial and permanent visual loss³.

Loss of vision is psychologically devastating and often causes a prolonged grieving reaction with shock, denial, anxiety, anger and depression. Psychological trauma is greater in young people who lose vision rapidly. The vast majority of diabetic individuals who lose vision do so ***not because of an inability to treat their disease, but rather due to a delay in seeking medical attention.***

The prognosis for diabetic retinopathy used to be dismal. Today, using timely laser photocoagulation as advocated by the Diabetic Retinopathy Study (DRS) and the Early Treatment Diabetic Retinopathy Study (ETDRS), severe visual loss can be reduced by 95%. Nevertheless, many diabetics still became legally blind because they are not regularly examined by an ophthalmologist. Prevention offers the most hope of diabetics. If blood glucose levels are aggressively controlled early and consistently in the disease, both the onset of retinopathy and the pace of its progression are significantly delayed².

The best predictor of diabetic retinopathy is the duration of the disease. There is a strong and consistent relationship between hyperglycemia and the incidence and progression of diabetic retinopathy. After 20 yr of diabetes, nearly all patients with type 1 diabetes and > 60% of patients with type 2 diabetes have some

degree of retinopathy⁴. However, it must be remembered that most patients are asymptomatic until the disease progresses to an advanced stage.

Regular examination and appropriate management can significantly reduce the risk of visual loss from diabetes mellitus. Better education, prompt diagnosis, and appropriate management could drastically reduce the morbidity from diabetic retinopathy and enhance the quality of life of patients for whom we care.

Classification and Characteristics

Diabetic retinopathy (Table-1) may be classified as nonproliferative or proliferative. Nonproliferative diabetic retinopathy (NPDR) is characterized by structural abnormalities of the retinal vessels (primarily capillaries but also venules and arterioles), varying degrees of retinal nonperfusion, retinal edema, lipid exudates, and intraretinal hemorrhages. Proliferative diabetic retinopathy (PDR) may include any of the changes present in nonproliferative disease with the additional findings of optic disc, retinal or iris neovascularization. Neovascular tissue contains both a vascular and fibrous components. The vascular components may cause preretinal or vitreous hemorrhage, and the fibrous components may interact with the vitreous to produce traction on the retina. Both NPDR and PDR may cause severe visual loss. The major vision-threatening complications include macular edema macular ischemia, neovascularization with preretinal or vitreous hemorrhage, retinal detachment, and neovascular glaucoma⁵.

Table 1: Early Treatment Diabetic Retinopathy Study Levels of Diabetic Retinopathy²

Nonproliferative Diabetic Retinopathy (NPDR)	
A. Mild NPDR	At least one microaneurysm Definition not met for B, C, D, E, F
B. Moderate NPDR	Hemorrhages or microaneurysms (H/Ma) are as bad as or worse than in standard photograph No. 2A Soft exudates, Venous beading (VB) and Intraretinal microvascular abnormalities (IRMAs) definitely present. Definitions not met for C, D, E, F
C. Severe NPDR	H/Ma more than in standard photograph No 2A in all 4 quadrants VB in 2 or more quadrants IRMA more than in standard photograph No.8A in at least 1 quadrant
D. Very Severe NPDR	Any two or more of C Definition not met for E,F Proliferation Diabetic Retinopathy
E. Early PDR	New vessels on the retina Definition not met for F

F. High-Risk PDR

New vessels on the disc (NVD) of $\frac{1}{4}$ to $\frac{1}{3}$ or more of the disc area or Any NV and vitreous or preretinal or

Any NV and vitreous hemorrhage Clinically Significant Macular Edema (any ONE of the following)

Thickening of the retina located 500 μm or less from the center of the macula

Hard exudates at 500 μm or less from the center of the macula with thickening of the adjacent retina. A zone of retinal thickening one disc area or larger in size, any portion of which is one disc diameter or less from the center of the macula

Presentation and Clinical Approach

It is vital to remember that even extensive proliferative changes may cause no visual symptoms, until vitreous hemorrhage or retinal detachment occurs. The absence of symptoms is therefore not necessarily reassuring, and the ever-present possibility of occult, potentially blinding retinopathy emphasizes the importance of routine screening and surveillance².

One of the early symptoms of diabetic retinopathy is poor night vision (dark adaptation) and poor recovery from bright lights (photostress). Also, diabetics, even those without retinopathy, are more likely to have abnormal color vision than are nondiabetics matched for age. Blue-yellow discrimination is affected earlier and more severely than is red-green discrimination. As retinopathy advances, color vision deteriorates³. Sudden painless loss of vision generally denotes an extensive vitreous hemorrhage or retinal detachment. A sparkling sensation, or distortion of the image in part of the visual field, may indicate retinal traction and herald detachment².

Patients with systolic or diastolic hypertension should have a baseline ophthalmologic examination at the time of diagnosis of diabetes mellitus. Patients with both younger-onset and older-onset diabetes who are taking insulin are most likely to progress to PDR if they have hypertension. Patients with proteinuria should be referred for baseline ophthalmologic examination at the time of diagnosis of diabetes mellitus. Hyperlipidemia has been associated with increased severity of intraretinal lipid exudates, which, in turn, is associated with worse visual acuity outcomes⁵.

The purpose of clinical examination are: (I) to assign each eye to one of the above categories of retinopathy; (II) to identify eyes at risk of visual loss, ideally loss, ideally before sight-threatening complications occur, and (III) to refer patients who need further assessment or treatment to the ophthalmic team (Table 2).

Table 2: Indications for referring a diabetic patients to an ophthalmologist²

Immediate referral: sight – threatening retinopathy

Proliferative retinopathy

New vessels on the optic disc

- New vessels else where in the retina
- Preretinal haemorrhage
- Fibrous tissue

Advanced diabetic eye disease

- Vitreous haemorrhage
- Fibrous tissue
- Recent retina detachment
- Rubeosis iridis / iris neovascularization

Early referral: Lesions likely to become sight – threatening within 1 year

Preproliferative retinopathy

- Venous irregularities (beading, reduplication, loops)
- Multiple haemorrhages
- Multiple cotton-wool spots
- IRMAs

Non-proliferative retinopathy with macular involvement

- Reduced visual acuity not corrected by pinhole (suggestive of macular edema)
- Haemorrhages and/ or hard exudates within one disc diameter of the macula, with or without visual loss.

Non-proliferative retinopathy without macular involvement

- Large circinate or plaque hard exudates within the major temporal arcades

Any other finding that the observer cannot interpret with reasonable certainty

Treatment of Diabetic Retinopathy

The systemic treatment of diabetic retinopathy includes control of factors that contribute to the pathogenesis of atherosclerosis and optimization of cardiac and renal function.

Glycemic Control

The Diabetes Control and Complications Trial (DCCT) demonstrated that tight glycemic control was associated with reduction in the onset and progression of diabetic retinopathy⁶. The findings were as follows:

1. Primary intervention group: Intensive therapy reduced the average risk of developing retinopathy by 76% (compared with conventional therapy).
2. Secondary intervention group: Intensive therapy reduced the average risk of progression of retinopathy by 54%(compared with conventional therapy). The risk of developing severe NPDR or PDR was reduced by 47%.

The United Kingdom Prospective Diabetes study (UKPDS), conclusively demonstrated that improved blood glucose control in patients with type 2 diabetes, reduces the risk of developing retinopathy and nephropathy and possibly reduces neuropathy. The overall microvascular complications rate was decreased by 25% in patients receiving intensive therapy versus conventional

therapy⁷. Epidemiological analysis of the UKPDS data showed a continuous relationship between the risk of microvascular complications and glycemia, such that for every percentage point decrease in HbA1c (e.g., 9 to 8%), there was a 35% reduction in the risk of microvascular complications.

In addition to accelerating large vessel atherosclerosis (as in the coronary, cerebral, and peripheral vasculature), hypertension has a deleterious influence on microvascular complications, including retinopathy and nephropathy.

Intensive insulin therapy in the type 2 diabetes has also been shown to reduce the risk of progression of retinopathy by 69% in the Kumamoto study⁸.

The effect of pregnancy on the eyes depends to a large extent on the status of the retinopathy at the beginning of the pregnancy. Certainly, pregnancy can accelerate the progression of diabetic retinopathy. Patients with mild NPDR frequently progress to more severe retinopathy, and 5% develop proliferative disease. About half of patients with proliferative disease at the onset of pregnancy develop more retinopathy during pregnancy if left untreated

All women with diabetes who becomes pregnant should have a baseline dilated fundus examination in their first trimester, and a complete dilated examination at least each trimester (every three months) (Table 3). If retinopathy is more severe at the outset, the frequency of examination should be increased appropriately⁴.

Table 3: Recommended Eye Examination Schedule for patients with Diabetes

Age of Onset of Diabetes Mellitus (years)	Recommended Time of First Exam	Recommended Follow-up*
0-29 [†]	5 years after onset	Yearly
30 and older [†]	At time of diagnosis	Yearly
Prior to pregnancy	Prior to conception or early in the first trimester	No retinopathy to nonsevere NPDR: every 3-12 months. Others stages of diabetic retinopathy every 1-3 months.

* Abnormal findings may dictate more frequent follow-up examinations.

[†] As indicated in Wisconsin Epidemiologic study of Diabetic Retinopathy, these are operational definitions of type 1 and type 2 diabetes based on age (age < 30 years at diagnosis, type 1; age > 30 years at diagnosis, type 2) and not pathogenetic classification.

Conclusion

Appropriate management of diabetic retinopathy can significantly reduce the risk of visual loss. The physician may help reduce the risk of visual loss by controlling blood pressure and blood glucose as well as possible. The ophthalmologist can offer laser photocoagulation surgery for diabetic macular edema or proliferative retinopathy and vitrectomy surgery for vitreous hemorrhage or severe, progressive neovascularization.

“He that is stricken blind cannot forget the precious treasure of his eyesight loss”.

Shakespeare : Romeo and Juliet

Management Recommendations for patients with Diabetes American Academy of Ophthalmology

Severity of Retinopathy	Ophthal Follow-up (months)	Focal Laser	Scatter (Panretinal) Laser	Fluorescein Angiography
1. Normal or minimal NPDR	12	No	No	No
2. Mild to moderate NPDR without macular edema	6-12	No	No	No
3. Mild to moderate DR with macular edema that is not clinically significant	4-6	No	No	Occasionally
4. Mild to moderate NPDR with CSME	2-4	Yes	No	Yes
5. Severe or very severe NPDR with no macular edema	3-4	No	Sometimes	Occasionally
6. Severe or very severe NPDR with CSME	2-4	Yes	Sometimes	Yes
7. Non-high-risk PDR with no macular edema	2-4	No	Sometimes	Occasionally

8. Non-high-risk PDR with CSME	2-4	Yes	Sometimes	Yes
9. High-risk PDR with no macular edema	3-4	No	Yes	Occasionally
10. High-risk PDR with CSME	3-4	Yes	Yes	Yes
11. High-risk PDR not amenable to photocoagulation	1-6	Not possible	Not possible	Occasionally
12. Very severe PDR	3-4	No	Yes	Yes

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Comments of Opinion Leaders:

"There is now an undisputable evidence favouring the 'Glucose Hypothesis' in the pathogenesis of diabetic microangiopathy. Data from Diabetes Control and Complication Trial (DCCT) in type 1 diabetes and the United Kingdom prospective Diabetes study (UKPDS) in type 2 diabetes show that the achievement of tight glycaemic control prevents or delays the progression of microvascular complications including diabetic retinopathy. This can be achieved with judicious combination of diet, exercise and drug treatment. Insulin treatment is crucial in patients who do not achieve tight glycaemic control with oral medications".

**- Dr. K. M. Shelgikar,
Pune**

"Both DCCT and UKPDS have shown in type 1 and type 2 diabetes subjects respectively, that achieving a near normoglycemia can prevent or retard the progression of chronic microvascular complications including diabetes retinopathy. We should strive to achieve a best possible glycaemic control in our diabetic subjects".

**- Dr. R.G. Naik,
Mumbai**

"Now that evidence are piling up on aggressive management of diabetes at very early stage in the natural course of disease. Such diabetic complications can be effectively prevented by tighter control of glycemic levels".

**- Dr. P. V. Rao,
Hyderabad**

"Diabetes is emerging as a major preventable cause of blindness in our country. It is the only diabetic complications that can be seen by the naked eye. The DCCT, UKPDS and Kumamoto studies have proved beyond doubt that tight glycaemic control significantly reduces onset and progression of diabetic retinopathy".

**- Dr. Shreerang Godbole,
Pune**