Diabetic retinopathy has been earmarked as one large pandemic which will have gross implications in India and all over the world by 2020. It has already grown into one of the biggest ocular problems in the developed nations. It is projected that India will overtake China as the single largest population of diabetics by 2025.

We can rest assured that diabetic retinopathy will be on the rise in the years to come.

Diabetic macular edema is the most common cause of diminution of vision among diabetics. In the Wisconsin epidemiologic study of diabetic retinopathy (WESDR), which is the largest epidemiologic study on diabetic retinopathy till date, it was documented that about 20% of IDDM patients and 25% of NIDDM patients on insulin will have macular edema after 10 years of diabetes.

In this short review we will go into the methods of diagnosis, evaluation and management of diabetic macular edema and chalk down the currently accepted practice patterns in the management of diabetic macular edema.

Macular Edema

1. Retinal thickening or hard exudates at or near the macula
2. Can be clinically significant or not
3. If clinically significant, has to be treated with photocoagulation
4. Can present with any grade of DR

Clinically Significant Macular Edema (CSME) (any one of the following):
1. Thickening of retina at or within 500 micrometer of the centre of the macula
2. Hard exudates at or within 500 micrometer of the centre of the macula if associated with retinal thickening of the adjacent retina
3. A zone or zones of retinal thickening of more than or equal to 1 disc area, any part of which is within 1 disc diameter of the centre of macula.

Evaluation of Diabetic Macular Edema

Direct ophthalmoscopy
Indirect Ophthalmoscopy
Hruby lens
Slit lamp aspheric indirect fundus biomicroscopy
Contact biomicroscopy
Fundus camera
Fluorescein Angiography
Optical Coherence tomography

Direct ophthalmoscopy

The direct ophthalmoscope gives a magnification of approximately 15 x and a field of view of 6.5 to 10 degrees, therefore, if we want to see more than just the very posterior pole the patient will have to look in 6 to 8 different directions. This 15 x magnification makes
the 1.5 mm disc appear much larger than it really is. The formula $M = \frac{60D}{4}$ holds well for up to + or - 10D’s of refractive error. The loss of stereopsis makes it a less beneficial tool in the diagnosis and management of diabetic retinopathy.

**Indirect ophthalmoscopy**

To view the fundus from the posterior pole to the periphery. With experience, can view the entire retina. Provides a minified, high resolution, stereoscopic view of the fundus. The magnification depends on the hand held lens used and in a trained hand it is a good method for the diagnosis, characterisation and management of diabetic retinopathy.

**Hruby lens**

The Hruby lens is available in both a contact and non-contact version. The non-contact Hruby lens is a high powered plano concave minus 55D which is available for most slit lamp biomicroscopes as an attachment from either above or below that can be rotated into the line of sight.

**Slit Lamp Aspheric Biomicroscopy (Indirect Fundus Lenses)**

These lenses have an advantage over the non-contact Hruby allowing a better view around cataracts. These lenses are double aspheric and come in +90D, +78D and +60D powers. The magnification increases inverse to the power of the lens. The +60 D lens gives greater magnification and is preferred by some for examination of the optic nerve and macula. The +90 D lens produces less magnification and larger field of view (30-40 degrees)

However, the slit lamp biomicroscope permits variable magnification which neutralizes this magnification problem.

The +78 D lens obviously falls in between the +60 D and +90 D lenses in terms of magnification and field view. It is slightly smaller in overall size than the +60 D and noticeably larger than the +90 D lens. The +78 D lens is usually preferred by the novice who feels it is easier to hold and manipulate

Magnification of the lens = power of the eye / power of the condensing lens

In a 90 D lens

$\text{Mag.} = \frac{60d}{90d}$

$\text{Mag.} = .666 \times$ magnification of slit lamp

Now a days, slitlamp biomicroscopy has become the gold standard in the diagnosis of diabetic macular edema.

**Contact biomicroscopy**

Contact biomicroscopy has superior resolution and stereopsis as compared with indirect lenses, but needs contact with the cornea and a coupling solution. It is done with a macular or posterior pole lens. As they are invasive and diabetic corneal epithelium is more amenable to damage, we do not usually retort to contact biomicroscopy routinely.

**Fundus photography**

Recently, fundus photography has been used for screening purposes using nonmydriatic cameras, which are designed to allow photography of the fundus through an undilated pupil. This has the potential benefit of permitting retinal evaluation without the need for pupillary dilatation, while providing a permanent record for later evaluation. However, these benefits are limited by the frequent difficulties of achieving adequate pictures through small pupils with cataracts. Obtaining useful photographs can be difficult, even for the experienced ophthalmic photographer, though the results can be improved by dilating the pupils. The results provided are two-dimensional, which makes evaluation of macular edema difficult. Because fundus photographs frequently depict extremely subtle pathologic change, these pictures must be analyzed by an ophthalmologist who is experienced at evaluating diabetic retinopathy. This technique should be used only as a screening method to help identify patients who may need more extensive evaluation using one or more of the techniques described.

**Fluorescein angiography**

Fluorescein angiography with color fundus photography is another useful method for evaluating diabetic
retinopathy. Stereoscopic color fundus photographs are first made of the macula and posterior peripheral retina of each eye. Then, the patient is given an injection of 5 to 10 ml of fluorescein dye intravenously. Rapid sequence photographs using filters matched to the spectral response of fluorescein in vivo are then taken immediately after injection of the dye and are continued periodically for 15 to 20 minutes. This technique can help determine the presence of capillary closure (which frequently cannot be determined by other clinical techniques), the presence of macular edema, the location of leaking microaneurysms and capillaries, and the presence of neovascularization. Fluorescein angiography provides a permanent record of the appearance of the fundus for later evaluation as necessary. The disadvantages of this technique include the need for dilation of the pupil, the need for intravenous injection of dye with its associated (though minimal) risk of an allergic reaction, and the additional cost.

**Indications of Fluorescein Angiography in Diabetic Macular edema**

1. To determine if retinal thickening in CSME is due to focal or diffuse leaks and to plan the photocoagulation treatment appropriately.
2. To identify ischemic maculopathy
3. To differentiate cystoid macular edema from diabetic macular edema in aphakes and pseudophakes.
4. To monitor the progression or regression of macular edema following macular photocoagulation

**Optical Coherence tomography**

OCT is a very convenient and accurate quantitative tool in the initial and sequential evaluation of diabetic macular edema. Its closest analogy in ophthalmology is like a visual field in glaucoma. We can have a very accurate anatomical reconstruction of the vitreomacular interface and that of the macula itself. The presence or absence of CME and vitreomacular traction can be easily picked up with this technique only. With the advent of intravitreal triamcinolone and other anti VEGF agents, OCT has become a very necessary tool. Other methods like the Retinal thickness analyzer (RTA) and HRT II has not become as popular as the OCT.

**Current practice patterns of evaluation**

Best corrected visual acuity
Dilated slitlamp biomicroscopy for diagnosis of CSME
If CSME present, then FFA is done
If CSME involves central fovea, suspicion of CME, suspicion of vitreomacular traction, then proceed for OCT.
Post laser residual CSME needs FFA and OCT
Unexplained visual loss requires OCT and FFA.

**MANAGEMENT OF CSME**

**Systemic factors**

Systemic factors like glucose levels, lipid levels and renal status play a role in the management of diabetic macular edema. The DCCT and UKPDS has demonstrated that glucose control and hypertension control will reduce the progression of diabetic macular edema. Other factors like stopping cigarette smoking and antioxidants have a marginal role in the control of progression.

**Laser photocoagulation**

The Early Treatment Diabetic Retinopathy Study (ETDRS) was a multicenter trial that showed a 50% reduction in visual loss in eyes with clinically significant macular edema treated with focal argon laser photocoagulation when compared with similar severity of edema in eyes not treated with laser photocoagulation. Photocoagulation for macular edema requires a recent (48-72 hours old) retinal fluorescein angiogram. Laser photocoagulation is directed specifically to the leaking macular microaneurysms noted angiographically. Multiple treatment sessions spread over many months are frequently necessary. Photocoagulation applied in a grid pattern surrounding the fovea may be useful for the management of zones of diffuse leakage or nonperfusion.

The ETDRS showed that focal photocoagulation should be considered for all eyes with clinically significant macular edema. In this study, focal photocoagulation treatment reduced the risk of moderate visual loss and increased the chance of visual improvement. The best timing for initiating treatment remains debatable for patients who have clinically significant macular edema
but are asymptomatic and have normal visual acuity. When considering the initiation of focal photocoagulation, the ophthalmologist must take into account the degree of central macular involvement, as well as the potential risk from photocoagulation. Potential side effects and complications of focal photocoagulation are unusual and include paracentral scotomata that frequently fade with time, development of abnormal neovascularization under the retina (subretinal neovascular membrane) that can lead to visual loss, and transient blurring of vision.

**Micropulsed diode laser**

The side effects of the focal macular photocoagulation are all caused by collateral and deep burns, and this is precisely what micropulse laser prevents. In this technique, laser is delivered in small trains or measures with sufficient time between these pulses so that the heat can be conducted. The results in diabetic macular edema has been encouraging with resolution in about 60% of eyes.

**Intravitreal steroids (IVTA)**

Intravitreal triamcinolone has been a very talked about treatment of diabetic maculopathy in recent times. It is an inhibitor of vascular endothelial growth factor and so it helps reduce the macular edema. It has proven its efficacy in residual macular edemas following one or two sittings of focal macular photocoagulation. Research is directed now to find if it is more effective in the primary management of diabetic macular edema even before laser. Though the results have been good, the selection of cases is of utmost importance. The eyes with a vitreomacular traction will worsen with an IVTA. Thus, it becomes imperative to study the vitreomacular interface before giving an IVTA.

IVTA is usually performed under topical anesthesia and with a 27 guage needle. 4 mg of preservative free triamcinolone is injected through the pars plana and tension controlled with paracentesis. This is done under aseptic precautions in the operating room.

Rise in IOP has been a limiting factor in intravitreal steroid administration. Though many cases are amenable to antiglaucoma drugs, as optic nerve in diabetes in very labile, this has to be managed aggressively. Other Complications associated with IVT injection of steroids include cataract progression, endophthalmitis, RD, hypotony, entrocular bleed etc.

**Pars plana vitrectomy**

It was found that an attached posterior hyaloid predisposed to the progression of diabetic macular edema, hence pars plana vitrectomy was tried for CSME. Early studies show good response to PVD induction and posterior hyaloid stripping in cases of CSME. Recent studies are concentrating on the effect of ILM peeling on diabetic macular edema. But as of now, PPV is done only in those cases with a documented vitreo macular traction on OCT with low vision. Since the complications of vitrectomy like cataract retinal tears and subsequent retinal detachments cannot be completely excluded, it is better avoided in eyes with vision better than 6/18.

**Futuristic trends**

Injection of anti VEGF agents (Intra Vitreal Injection of Pegaptanib (Macugen)
Chemical PVD
Protein kinase Inhibitors
COX 2 inhibitors
Extended release implants through parsplana (Flucinolone Implant)

**Conclusion**

All patients of diabetic macular edema should be encouraged to optimize treatment of systemic risk factors, be it glycemic control, lipid control or renal stabilization. Blood pressure control should be emphasized upon and patient is asked to quit smoking. In presence of renal dysfunction, it is important to initiate the patient on ACE inhibitor also.

After this is done, in majority of patients focal macular photocoagulation direct to microaneurysms picked up on fluorescein angiography should be performed during the first sitting. Do not go closer than 350 microns of the center of the fovea.

Wait for 3 to 4 months before any other intervention. After that, the patients are assessed regarding any
residual macular edema with fluorescein angiography and OCT in select cases. If there are still microaneurysmal leakage, a second sitting of macular laser, this time going more closer to the fovea if needed is done. In select patients in whom, there is recalcitrant macular edema even after 2 sittings of focal macular laser, 4 mg of triamcinolone intravitreally is advised, provided, the patient completely understands the efficiency and consequences of the procedure. After IVTA, a fluorescein angiography is repeated at 2 months to look for any possible microaneurysms which are amenable to treatment.

In those patients who have failing vision over 6 months and in whom a vitreomacular traction has been demonstrated on OCT, pars plana vitrectomy can be advised. However it is undertaken only if the patient understands the nature of treatment and its efficacy and side effects.

With this approach, we are able to satisfactorily treat the majority of patients with CSME. When ever possible, the least aggressive approach is utilized. The newer approaches to diabetic macular edema looks promising but need large clinical trials & long term followup studies to assess their efficacy.