Current trends and challenges for management of Diabetic Retinopathy in India

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With the global epidemic of lifestyle-induced diseases, Diabetes Mellitus (DM), amongst others, is a major looming threat in India. The number of diagnosed cases is increasing steadily, leading to the challenge of management of complications, namely renal, ocular, and neurological complications. A multidisciplinary approach is required, with combined efforts by physicians, nephrologists, and ophthalmologists to provide comprehensive care to a diabetic patient.

Diabetic Retinopathy

Amongst the various complications of DM, Diabetic Retinopathy (DR) causes severe visual morbidity and remains largely underdiagnosed. It is one of the leading causes of avoidable blindness, warranting screening and early intervention for a favorable visual prognosis. The Wisconsin epidemiological study of Diabetic Retinopathy found the incidence rates of Diabetic Macular Edema (DME) to be 20% in patients with Type 1 DM and between 14 and 25% in patients with Type 2 DM of more than ten years[(1)].

India has approximately 77 million people with diabetes, and these numbers are predicted to increase to 125 million by 2045[(2)]. The rate of blindness due to diabetic retinopathy will also increase with this exponential rise in the prevalence of diabetes. Rajendra Prasad (RP) Center for Ophthalmic Sciences conducted the National Diabetic Retinopathy Rapid Assessment of Avoidable Blindness (RAAB) Survey 2015–2019 under the aegis of the Ministry of Health and Family Welfare (MoHFW), Government of India. The prevalence of DR among diabetics was found to be 16.9%[(3)].

DR develops in patients having diabetes for more than 5 years. Occurrence of DR has been found to be proportional to duration as well as control of diabetes. Chronic hyperglycemia causes oxidative damage to the vascular endothelial cells and leads to ischemia. Following this, a variety of growth factors, insulin-like growth factor-1, fibroblast growth factor-2, tumor necrosis factor, and Vascular Endothelial Growth Factor (VEGF) are overexpressed. VEGF mediates angiogenesis, protease production, endothelial cell proliferation, migration, and neovascularization[(4)].

Clinically, early DR goes through a mild and nonproliferative stage. The retina shows changes in form of microaneurysms and retinal hemorrhages. The patient may not experience any visual problem, however the disease may later progress to Vision-Threatening Diabetic Retinopathy (VTDR) marked by severe proliferation leading to vitreous hemorrhage, retinal detachment and development of macular edema. Diabetic Macular Edema (DME) is the leading cause of visual dysfunction in the diabetic population.

Standard ophthalmic screening involves fundus examination, including fundus photography and Optical Coherence Tomography (OCT) and/or Fundus Fluorescein Angiography (FFA).

Treatment trends

Patients with early DR may not require specific ocular treatment, but only glycaemic control and periodic follow-ups. Patients showing evidence of macular edema or neovascular proliferation are considered for immediate treatment.

Lasers have been the gold standard for the treatment of DR. Converting the hypoxic areas of the retina to anoxic areas to reduce the secretion of vascular proliferative growth factors is the principle of this treatment. Reduction in macular edema is achieved by low-power laser application in the form of a grid or as focal laser targeting leaking microaneurysms. The proliferative phases warrant pan-retinal coagulation to achieve regression of new vessels and arrest progression[(5)]. Advanced stages with extensive proliferation and tractional retinal detachment are treated by vitrectomy and endolaser. Laser treatment helps to arrest the progression of the disease but causes no improvement in vision. The Pattern Scan Laser (PASCAL) is a new system of laser delivery allowing choosing from a variety of arcs, circular grid patterns, and grid sectors, or employing a rectangular array. Navigating laser treatment (NAVILAS) is a recent technology that uses integrated imaging and navigation technology for image-guided navigated laser delivery.

However, the current scenario of DR management has drastically changed with the emergence of Anti-VEGF drugs and ushered in an era of intravitreal pharmacotherapy. Anti-VEGFs are a variety of distinct compounds, including

aptamers (i.e., Pegaptanib), antibodies to VEGF (i.e., Bevacizumab), antibody fragments against VEGF (i.e., Banibizumab), and fusion proteins (i.e., Aflibercept and new drug brolucizumab, is a single-chain antibody fragment[6]. All these drugs cause reduction in VEGF activity thus reducing vascular permeability and neovascularization. Anti-VEGF medicines are now regarded as the first line of therapy in center involving DME. The big challenge with Anti-VEGF therapy is its cost. As patient may require multiple injections, it can be a financial burden. The introduction of anti-VEGF biosimilar drugs produced in India has significantly reduced the treatment cost.

Corticosteroids have been used along with laser treatment for treating DME. They cause stabilization of the blood–retina barrier, reduction in capillary permeability, and enhance the endothelial tight junction activity. Currently available corticosteroids for the treatment of DME include intravitreal triamcinolone acetonide, dexamethasone intravitreal implant, and fluocinolone acetonide intravitreal inserts. However, long-term intravitreal steroid implants carry the risk of causing raised intraocular pressure[6].

Combination therapy using lasers and Anti-VEGF/corticosteroids primarily helps to lengthen the duration of the anti-VEGF action and minimize the number of injections, which may assist in reducing the treatment burden. On the future horizon are trials of drugs like Faricimab, which is a Cytokine inhibitor[6].

Vitreoretinal surgery is the only option for cases of nonresolving vitreous haemorrhage and / or tractional retinal detachment.

The visual outcome in advance cases of diabetic retinopathy is often very poor inspite of treatment.

Challenges and solutions

Systematic screening of the diabetic population has been shown to greatly reduce the prevalence and incidence of blindness within the population[7]. An integrated DR screening and management program within our healthcare system is needed. Currently, the National Program for Control of Blindness (NPCB) has an opportunistic screening of DR in a high-risk population in India, which emphasizes early diagnosis, referral, and management at every possible point of contact of the patient with the healthcare provider. India has demographic as well as socioeconomic variations, and the disease burden varies across states. Implementation of systematic screening and treatment pathways for diabetic retinopathy need to be stratified accordingly[8].

In the urban scenario, facilities for diagnosis and treatment are available at most tertiary centers with specialists in medical as well as surgical vitreo retina practice. Yet lack of awareness of ocular morbidity in diabetic patients remains a major challenge faced by ophthalmologists. Information and counseling regarding the regular ocular examination are essential to identify DR at early stages, to treat it in order to prevent loss of vision. Patients with DR do not experience symptoms until the advanced stages of the disease and therefore fail to seek an appointment with an ophthalmologist. Sadly, the treating physician often does not insist on an ophthalmological exam. Praveen et al. have shown the feasibility of a comprehensive DR screening model even at the tertiary diabetic care facility[9]. This consists of comprehensive DR screening at the diabetic clinic, patient education sessions, and annual follow-up screening camps for the detection of diabetic complications. A general physician or the diabetologist can also make use of customized artificial intelligence-based systems to easily identify patients needing referral and timely cross-reference to a retina expert.

Although diabetes is twice more frequent in the urban population compared with the rural, providing diagnostic and treatment options to the rural population is a challenge. No access to screening or diagnostic facilities in the vicinity, followed by the cost of travel remain barriers to early diagnosis and treatment. The All India Ophthalmology Society (AIOS) and Vitreo-Retinal Society of India (VRSI) have initiated several measures to improve DR screening in India. They have created guidelines and suggested strategies for screening and managing DR, both at hospitals and through community outreach[10]. Outreach programmes like screening camps and awareness campaigns can be very valuable to reach out larger populations. Educational and awareness modules for the training of various healthcare providers, including hospital staff, local pharmacists and Accredited Social Health Activists (ASHA) workers may be very useful to motivate patients.

Teleophthalmology helps to overcome the paucity of experts available. Screening can be done by technicians by taking stereoscopic fundus photographs with a fundus camera. Monitoring the tele-screening program, image interpretation, providing knowledge and skills to image readers, can be done by Ophthalmologist with expertise in DR. Well-equipped mobile vans manned by health care staff trained in the use of portable fundus cameras, and teleophthalmology software, can be made available to reach a large population. Mobile eye vans may also be used to administer treatment at primary levels by a visiting Opthalmologist. Efficient referral system and patient counselling is also of paramount importance, as it has been noted that only half of the referred patients actually report to higher centers[11,12].

Patient education and screening can help detection of diabetic retinopathy in and early stage. Early diagnosis and treatment will help in preventing blindness. Good control of diabetes,

lifestyle changes, and regular retinal examination will help prevent sight-threatening disease. This emphasizes the need for coordinated efforts among all healthcare workers, physicians, and ophthalmologists. We can look forward to technology in the form of Artificial Intelligence (AI) which could be a boon in developing easy-to-use models for early diagnosis of diabetic retinopathy.

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