Guest Editorial

Diabetic retinopathy: Battling the global epidemic

In 1969, William Beetham published his work in the journal, Transactions of the American Ophthalmological Society about the efficacy of ruby laser in patients with proliferative diabetic retinopathy (PDR).[1] Encouraged by these findings, the Diabetic Retinopathy Study, a National Institute of Health-sponsored landmark clinical trial confirmed the benefits of the panretinal photocoagulation (PRP) laser in PDR patients. Since then, the argon PRP laser became the main-stay treatment in these patients. In the same paper, the authors attributed the successful results to the "reduction in the functioning retina., or the vasoformative factor, or both." Later this vasoformative factor proved to be vascular endothelial growth factor (VEGF) and was targeted in many clinical trials in different retinal diseases. Almost four decades later, another landmark clinical trial, Diabetic Retinopathy Clinical Research Network just published that monthly anti-VEGF injections are no inferior to the gold standard PRP laser treatment and have the advantages of no visual field loss seen with the PRP laser.[2] Thus, we have now two effective evidence-based treatments available for regression of retinal neovascularization in PDR patients. Many other large randomized trials in diabetic retinopathy (DR) in between have taught us how to treat DR patients effectively in DME, PDR, and even in early stages of DR. Ophthalmologists have now several novel drugs including anti-VEGF drugs and steroid implants available in their armamentarium for treating patients with DME and PDR. Many more drugs are in the pipeline in different phases of clinical trials.

In spite of all the advances we have seen, diabetes still remains to be rampant throughout the world and has assumed the proportions of a global epidemic. According to the International Diabetes Federation, the number of diabetics in the world today is 387 million, and this number is being projected to increase to 592 million by 2035.[3] Every 7 s, one person dies from diabetes somewhere in the world. India ranks second in the prevalence of diabetes globally (with 67 million diabetics). With the increase in the incidence of diabetes, its microvascular complication retinopathy has also increased accordingly. It is the leading cause of blindness in middle-aged adults. With these alarming changes in mind, this issue of IJO has assembled a panel of experts who have reviewed the update on a wide number of areas including epidemiology, diagnostic imaging, control of systemic factors, genetic factors, laser therapy, novel pharmacotherapies, and telemedicine in the management of DR.

Diabetes caused about five million deaths and 612 billion dollars cost in health expenditure in 2014.[3] This cost is further rising. Raman *et al*. in this issue describe this impact of diabetes in India as well as globally.[4] The role of tight glucose control in prevention and slowing down the progression of DR has been proved in many landmark clinical trials including Diabetes Control and Complications Trial (DCCT), United Kingdom Prospective Diabetes Study, Epidemiology of Diabetes Intervention and Complications, and the recent Action to Control Cardiovascular Risk in Diabetes (ACCORD) Study. However, the ACCORD study also points out that too tight control might result in serious cardiovascular consequences. Mohan *et al*., give their insight into the role of control of systemic factors in the management of DR from the diabetologist's point of view.[5]

Diabetes is a multifactorial disease, and the role of genetic factors in the pathogenesis of DR has been attributed to also in some sporadic studies. The DCCT study has shown familial clustering of severe retinopathy among the first-degree relatives. Mishra *et al*. have reviewed the current status of genetic studies in relation to DR, and stress how the next generation and high input genomic technologies can advance the field.[6] In the field of diagnostic imaging tools, the optical coherence tomography (OCT) is another fast, convenient, highly reproducible tool for quantitative measurement and mapping of macular thickening, and indispensable in measuring the outcomes of treatment with anti-VEGF drugs. Tan and Sadda discuss the importance of OCT and other advanced imaging modalities in managing patients with DR.[7]

With the introduction of anti-VEGF agents, the treatment paradigm for DR has changed drastically. Several anti-VEGF drugs, as well as steroid implants, have been approved by the FDA in DR patients. However, the response to these drugs is variable, as factors other than VEGF may play significantly in the alteration of the blood-retinal barrier. The review on pharmacotherapies summarizes the clinical trials involved in the use of these drugs and describes future directions in the coming years.[8]

Telemedicine is a unique approach in having an immediate access and meeting the vast demands of screening of diabetic populations. Clinical examinations alone are unlikely to meet the needs of screening of this disease. Das and Pappuru emphasize this need in their article and describe how this strategy can be cost-effective for battling this epidemic.[9] As pointed out earlier, control of systemic factors is crucial in the management of DR patients. There is an urgent need for an integrated approach where eye care and diabetes care can go under one roof with one goal of improving the quality of life of diabetics. Murthy and Das have stressed this diabetes care initiative in India in their comprehensive review.[10]

Over the last five decades, we have seen tremendous advances in the management of DR. We have learned from large, randomized clinical trials that tight control of blood glucose, blood pressure, and blood lipids in the early stage of diabetes is critical in preventing and slowing down the progression of DR. We have learned about novel pharmacotherapeutic approaches in the visual improvement of patients who would otherwise go blind from this disease. We will see many more novel drugs targeting the inflammatory cascade, novel drug delivery systems, nanotechnology, neuroprotective agents, and stem cell therapy with endothelial progenitor cells in promoting repair of blood vessels and reperfusion of ischemic areas. Still, we need to better understand the pathogenesis of DR. What are the role of genetic factors in DR? What does determine the anti-VEGF

responsiveness? What are the factors beyond VEGF involved in DR? The question that remains challenging is that how we battle this global epidemic in the coming years. Given the alarming nature of this epidemic, we need an integrative approach to fight against this devastating disease.

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References

1. Beetham WP, Aiello LM, Balodimos MC, Koncz L. Ruby-laser photocoagulation of early diabetic neovascular retinopathy: Preliminary report of a long-term controlled study. Trans Am Ophthalmol Soc 1969;67:39-67.
2. Writing Committee for the Diabetic Retinopathy Clinical Research Network, Gross JG, Glassman AR, Jampol LM, Inusah S, Aiello LP, *et al*. Panretinal photocoagulation vs. intravitreous ranibizumab for proliferative diabetic retinopathy: A Randomized Clinical Trial. JAMA 2015;314:2137-46.
3. International Diabetes Federation. IDF Diabetes Atlas. 6th ed. Brussels, Belgium: International Diabetes Federation; 2014.
4. Raman R, Gella L, Srinivasan S, Sharma T. Diabetic retinopathy: An epidemic at home and around the world. Indian J Ophthalmol 2016;64:69-75.
5. Rajalakshmi R, Prathiba V, Mohan V. Does tight control of systemic factors help in the management of diabetic retinopathy?. Indian Journal of Ophthalmology 2016;64:62-8.
6. Mishra B, Swaroop A, Kandpal R. Genetic components in diabetic retinopathy. Indian J Ophthalmol 2016;64:55-61.
7. Tan CS, Chew MC, Lim LW, Sadda SR. Advances in retinal imaging of diabetic retinopathy and diabetic macular edema. Indian J Ophthalmol 2016;64:76-83.
8. Das A, McGuire PG, Monickaraj F. Novel Pharmacotherapies in diabetic retinopathy: Current status and what's in the horizon? Indian J Ophthalmol 2016;64:4-13.
9. Das TP, Pappuru RR. Telemedicine in diabetic retinopathy – Access to rural India. Indian J Ophthalmol 2016;64:84-6.
10. Murthy GV, Das TP. Diabetic care Initiatives to prevent blindness from diabetic retinopathy in India. Indian J Ophthalmol 2016;64:50-4.

Access this article online	
Quick Response Code:	**Website:** www.ijo.in
	DOI: 10.4103/0301-4738.178155

Cite this article as: Das A. Diabetic retinopathy: Battling the global epidemic. Indian J Ophthalmol 2016;64:2-3.