Commentary: From diabetic retinopathy toward diabetic retinal disease

In the year 2018, Abramoff MD and colleagues from the University of Iowa, United States came up with a new term to describe retinal involvement in diabetes mellitus.[1] They proposed that the term "diabetic retinal disease" should be used instead of "diabetic retinopathy." Their assertions were based on the fact that the existing classification of diabetic retinopathy does not take into account newer imaging characteristics and newer pathophysiological insights into retinal involvement in diabetes mellitus. By the newer imaging characteristics, they meant ultra-widefield retinal imaging and high-resolution optical coherence tomography. It is noteworthy that the Early Treatment Diabetic Retinopathy Study focused only on the 75 degree of the posterior pole of the retina. They further argued that standard use of optical coherence tomography in the management of diabetic retinopathy has been limited to measurement of central macular thickness and correlating it with treatment response, whereas recent qualitative markers such as disorganization of inner retinal layer, photoreceptor length, and the integrity of the external limiting membrane and ellipsoid zone are yet to find suitable representation in the diabetic retinopathy classification system. The assessment of neuroretina with optical coherence tomography was an additional aspect that they found underutilized especially with the recent body of developing evidence which suggests that retinal neuropathy may coexist or even precede the development of retinopathy in diabetes mellitus. Diabetic retinal neuropathy is the term that encompasses the neural changes in the retina seen in eyes with diabetes mellitus.[1,2] It includes alterations in the structure such as neural apoptosis, ganglion cell loss, gliosis, and inner retinal thinning. The functional effects of these changes on dark adaptation, color, and contrast sensitivity are captured by electroretinogram, microperimetry, and other respective investigations. They suggested further studies incorporating diabetic retinal neuropathy changes along with diabetic retinopathy under a broad term of diabetic retinal disease.

It is indeed real that the current management of diabetic macular edema is mainly aimed toward reduction in central macular thickness. However, a reduced or restored anatomy of the macula does not always lead to improvement or restoration of visual acuity. Ongoing diabetic retinal neuropathy has been linked to suboptimal visual gain in spite of successful treatment of diabetic macular edema.[3] An increasing body of evidence suggests that diabetic retinal neuropathy may be present in eyes with no clinical retinopathy.[1-3] However any possible causal association between neuropathy and retinopathy is still in the realms of future research.[1] Diabetic retinopathy has been considered as a marker of systemic neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease, which further emphasizes the significance of diabetic retinal neuropathy as a component of diabetic retinal disease.[4]

Photopic negative response (PhNR) in full filed electroretinogram is a marker of retinal ganglion cell activity.[5] Loss of retinal ganglion cells is an integral aspect of diabetic retinal neuropathy and it was imperative that PhNR would have been studied in detail prior to the present study. However, the present study adds value to the existing body of literature by using both broadband (white on white) and monochromatic (red on blue and blue on yellow) PhNR and correlating them with various stages of diabetic retinopathy.[6] Authors report a significant reduction in both broadband and monochromatic PhNR amplitudes in eyes with diabetes mellitus compared to healthy controls. This difference was present even in eyes that did not have clinical diabetic retinopathy, and it buttresses the hypothesis that diabetic retinal neuropathy precedes clinical diabetic retinopathy. They further noted that the extent of reduction in the PhNR amplitudes correlated linearly with the severity of diabetic retinopathy, and it was more prominent with monochromatic blue on yellow PhNR. S cone pathways are affected earlier than L and M cone pathways in diabetic retinopathy.[7] S cone pathways are mainly responsible for blue on yellow PhNR, explaining its significant and earlier involvement in the spectrum of diabetic retinopathy. The present study is important because it opens up newer avenues for early risk stratification of future development of retinopathy in diabetic individuals. Reduction in PhNR amplitude, especially the monochromatic blue on yellow, has the potential of being used as a marker of the development of diabetic retinopathy. However, such an application would require further validations with a larger sample size in a longitudinal study design.

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