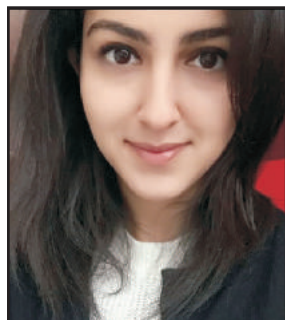


Retinal Nerve Fibre Layer Involvement In Diabetic Retinopathy

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Introduction:

Diabetic retinopathy (DR) is a progressive microvascular complication of diabetes due to which irreversible retinal damage can occur. This is the leading cause of vision loss in working-age adults (20-65 years) and, therefore, professionally active people.^{1,2}

Optical Coherence Tomography And Retinal Nerve Fibre Layer:

Spectral domain optical coherence tomography (SD-OCT) imaging has proven to be an effective tool for detecting the earlier stages of the disease, tracking progression, and monitoring treatment response in case of diabetic retinopathy.³ Extensive research has correlated OCT based retinal thickness with visual acuity in diabetic macular edema.^{5,6}

Association of retinal nerve fibre layer (RNFL) thinning with severity of type 2 DR on SD-OCT has been shown.⁷ Progression of DR and poor glycemic control is related to RNFL thinning.^{8,9}

Various studies have shown a reduction in the inner retinal thickness in the macula in diabetics with mild DR, which may suggest initial ganglion cell loss in the pericentral areas and RNFL thinning.^{13,14}

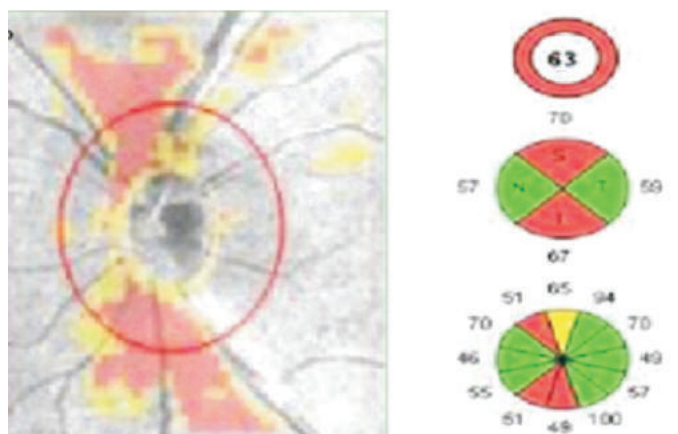


Figure 1: Retinal Nerve Fibre Layer (RNFL) thickness analysis using optic disc cube 200 × 200 feature depicting RNFL thinning in proliferative diabetic retinopathy

Rodrigues et al.¹² documented that neuroretinal changes occur before vascular changes ensue in diabetes mellitus. They noted a significant thinning of ganglion cell layer (GCL) and RNFL in patients with diabetes mellitus with no DR.

Pathophysiology Of Diabetic Retinopathy and Subsequent Rnfl Changes

Neurogenic Changes

Diabetic retinopathy, previously considered as a solely vascular disease, is now recognized as a neuro-vascular disease. Retinal neurodegeneration has been found to have a significant role in the pathogenesis of DR, including apoptosis of retinal neuronal cells and peripapillary retinal nerve fibre layer (RNFL) thinning.¹⁶ Thus, we need to rule out the presence of glaucoma in such patients showing RNFL thinning.

The hypothesis given by Rodrigues et al.¹² showing that neuroretinal changes occur before vascular changes ensue in diabetes mellitus has been confirmed by electrophysiological and psychophysical studies.¹⁷

Vascular Changes

Basement membrane thickening, pericyte loss,¹⁹ oxidative and nitrosative stress,²⁰ and decreased capillary perfusion lead to retinal capillary endothelium damage. This results in fluid leakage out of the capillaries resulting in DME, capillary closure and decreased capillary blood flow. These changes give rise to decreased blood supply to retina with resultant retinal ischemia and increased vascular endothelial growth factor (VEGF) release.^{21,22} Administration of intra-vitreous anti-VEGF causes decrease in severity of DME.

Central retinal artery (CRA) supplies the inner 6 layers of retina. Resistive Index (RI), a parameter of vascular resistance, changes with the severity of DR. Increase in RI of CRA, related to the vascular endothelium damage, was found to correlate significantly with severity of retinopathy as well as decrease in RNFL thickness in our previous studies.²³

Role Of Homocysteine

Homocysteine is a by-product of transmethylation reactions and is detoxified by methionine synthetase, which requires vitamin B12 and folate as coenzymes for proper function. Raised total plasma levels of homocysteine has been established to be an independent risk factor for retinal vascular occlusive disease.²⁴ Homocysteine, by inducing apoptosis in

retinal ganglion cells due to the expression of Bax, a proapoptotic protein, contributes to the development of diabetic retinopathy.²⁵ In our previous studies we have been able to demonstrate a correlation between increased serum levels of homocysteine and in vivo retinal nerve fibre layer thinning in the diabetic retina associated with an increased severity of retinopathy.²⁶ Therefore, strategies for controlling the level of homocysteine by supplementation with folic acid or vitamin B12 may be potential treatment approach to amend neurodegeneration.

Take Home Messages

- 1) Neurogenic changes precede vascular changes in diabetic retinopathy, therefore diabetics with normal fundus findings on examination should be followed up with OCT–RNFL at regular intervals.
- 2) Color doppler is an easy, inexpensive way to screen patients with DR as RI correlates with RNFL thinning.
- 3) Serum homocysteine should be done for all patients of diabetic retinopathy and any derangements should treated with folic acid and vitamin B12 supplementation in consultation with a physician.

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