Section: Miscellaneous

Original Research Article

RETINAL NERVE FIBRE LAYER CHANGES IN DIABETIC PATIENTS: INSIGHTS FROM A CROSS-SECTIONAL STUDY IN KERALA

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ABSTRACT

Background: Diabetic retinopathy (DR) is traditionally regarded as a microvascular complication, but increasing evidence suggests that retinal neurodegeneration, particularly retinal nerve fiber layer (RNFL) thinning, may precede visible vascular changes. The objective is to estimate RNFL thickness in diabetic patients with and without retinopathy compared to non-diabetic controls, and to identify clinical predictors of RNFL thinning in a hospital-based population in Kerala.

Materials and Methods: This cross-sectional study included 123 participants (41 controls, 41 diabetics without DR, and 41 diabetics with DR). Peripapillary RNFL thickness was measured using spectral-domain OCT. Clinical data, including age, gender, duration of diabetes, and HbA1c, were collected. Group differences were analyzed using ANOVA, and predictors of RNFL thinning were assessed using linear regression.

Results: Mean global RNFL thickness was significantly reduced in diabetic patients with DR (92.1 ± 8.3 µm) compared to diabetics without DR (98.4 ± 9.1 µm) and controls (101.7 ± 7.8 µm, $p<0.001$). Superior and inferior quadrants showed the most pronounced thinning. Regression analysis revealed age ($\beta = -0.32$, $p<0.001$) and duration of diabetes ($\beta = -0.28$, $p = 0.002$) as independent predictors of RNFL thinning. HbA1c, though elevated in DR patients, was not a significant independent predictor after adjusting for duration.

Conclusion: RNFL thinning occurs in diabetic patients, more prominently in those with DR, indicating a neurodegenerative component of diabetic retinal disease. Age and duration of diabetes emerged as key predictors of RNFL loss, while the role of HbA1c appears indirect through its correlation with disease chronicity. These findings highlight the importance of incorporating RNFL assessment into early screening strategies for diabetes-related ocular complications.

Keywords: Diabetes mellitus, diabetic retinopathy, retinal nerve fibre layer, optical coherence tomography, neurodegeneration, RNFL thinning, early detection.

INTRODUCTION

Diabetes mellitus (DM) is a common, chronic metabolic disorder that develops over a long period and is characterized by gradual hyperglycemia due to defects in insulin secretion, insulin action, or both.[1] In 2021, the estimated number of adults with diabetes worldwide was 537 million, projected to rise to 643 million by 2030.[2] India, the new diabetes capital of the world, is carrying a considerable share of this burden, with increasing prevalence even in urban and rural populations.[3]

One of the most prevalent microvascular complications of diabetes is DR, which continues to

be a significant cause of preventable blindness and visual impairment among the productive adult population.[4] DR has been chiefly considered a microangiopathy of retinal capillaries characterized by vascular permeability, ischemia, and neovascularization.[5] Nevertheless, more recent findings from ocular imaging and neurobiology have questioned this hypothesis and proposed an earlier involvement of retinal neurodegeneration in diabetic retinal disease.In diabetes, a topographical loss of the RNFL, which is almost exclusively composed of ganglion cell axons, puts these compartments under considerable metabolic and oxidative stress.[6] Newer evidence from preclinical research suggests that RNFL thinning may precede clinically detectable retinopathy by years and serve as an early biomarker for diabetic retinal changes.[7] For instance, spectral-domain optical coherence tomography (SD-OCT) has enabled a high-resolution and non-invasive measurement of RNFL for objective determination of neurodegenerative alterations presumably preceding clinical signs of vascularity.[8]

Although many international studies have reported RNFL thinning in patients with diabetes without retinopathy, such data are scarce from India, particularly among regional hospital-based populations.[9]Glycemic control, duration of diabetes, age, and comorbidities are also regarded as possibly exerting a systemic influence on RNFL thickness to varying and contradictory extents among studies.[10]This study was conducted to estimate RNFL thickness in diabetic patients with or without retinopathy compared to non-diabetic controls in a hospital-based population of Kerala. We also intended to find clinical predictors of RNFL thinning, such as age, gender, HbA1c, and duration of diabetes. Several studies have investigated potential predictors of RNFL thinning, including age, duration of diabetes, glycemic control (HbA1c), and the presence or absence of diabetic retinopathy. We hope to understand this neurodegenerative component of diabetic retinal disease even better by mapping the structural changes in the retina that may occur at different stages of diabetes and contribute to early screening strategies. Understanding these neurodegenerative changes and their clinical determinants may enhance early screening strategies in populations with a high burden of diabetes, such as Kerala.

MATERIALS AND METHODS

Study Design and Setting: A cross-sectional observational study was conducted in a tertiary care center, a hospital-based in Kerala, India. The study aimed to evaluate RNFL thickness in diabetic patients with and without DR compared to age-matched non-diabetic controls. The Institutional Ethical Clearance Committee reviewed and approved the study, and all participants provided written informed consent, as required by the Declaration of Helsinki.

Study Population: A total of 123 subjects were enrolled and categorized into three groups:

- Group 1 (Control): Non-diabetic individuals without retinopathy (n = 41).
- Group 2 (Diabetes without DR): Patients with diabetes but no evidence of DR on fundus examination (n = 41).
- Group 3 (Diabetes with DR): Patients with clinically diagnosed DR (n = 41).

Inclusion criteria were adults aged 30–70, diagnosed cases of type 2 diabetes mellitus for ≥1 year in diabetic groups, and healthy non-diabetic individuals as controls. Exclusion criteria included glaucoma, ocular hypertension, optic neuropathies, media opacities interfering with imaging, high refractive errors (> ±6D), or systemic neurological diseases.

Clinical and Laboratory Assessment: Demographic details (age, gender), duration of diabetes, and relevant medical history were collected. Glycosylated hemoglobin (HbA1c) levels were measured using standardized laboratory methods. All participants underwent best-corrected visual acuity (BCVA), slit-lamp biomicroscopy, intraocular pressure measurement, and dilated fundus examination. DR staging was performed based on the Early Treatment Diabetic Retinopathy Study (ETDRS) criteria.

Optical Coherence Tomography (OCT) Imaging: Peripapillary retinal nerve fibre layer (RNFL) thickness was measured using spectral-domain OCT (NIDEK RS-330). A circular scan of 3.4 mm around the optic disc was performed, and global and quadrant-wise (superior, inferior, nasal, temporal) RNFL thickness values were recorded. Scans with signal strength <7 or with segmentation errors were excluded.

Statistical Analysis: Data were analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation (SD). Group comparisons were performed using one-way ANOVA with post hoc Tukey's test for continuous variables and chi-square test for categorical variables. Correlation between RNFL thickness and clinical variables (age, duration of diabetes, HbA1c) was assessed using Pearson's correlation. Multiple linear regression analysis was performed to identify independent predictors of RNFL thinning. A p-value <0.05 was considered statistically significant.

RESULTS

Participant Demographics: A total of 123 participants were included: 41 controls, 41 diabetics without DR, and 41 diabetics with DR. The mean age across groups was comparable ($p > 0.05$). HbA1c levels were significantly higher in both diabetic groups thanin controls ($p < 0.001$). The

mean duration of diabetes was longer in the DR group than the no-DR group ($p < 0.01$).

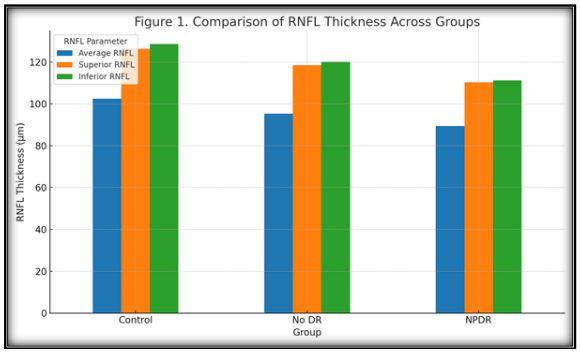
Table 1: Baseline demographic and clinical characteristics of study groups

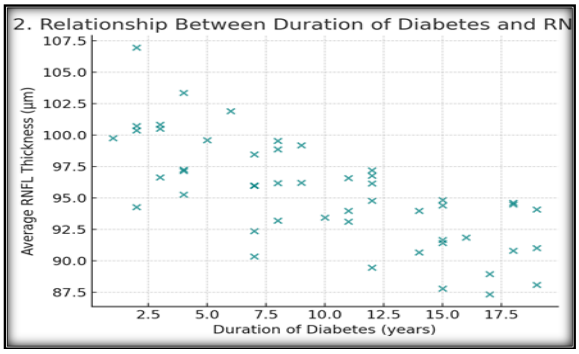
Parameter	Control (n=41)	No DR (n=41)	DR (n=41)	p-value
Age (years)	52.4 ± 8.6	53.1 ± 9.2	54.6 ± 7.9	>0.05
Duration of diabetes (years)	-	6.2 ± 2.1	9.4 ± 3.0	<0.01
HbA1c (%)	5.2 ± 0.4	7.8 ± 0.9	8.9 ± 1.1	<0.001

RNFL Thickness Across Groups: Mean global RNFL thickness was highest in controls (100.4 ± 7.8 µm), followed by the no-DR group (95.7 ± 8.1 µm) and lowest in the DR group (90.9 ± 8.5 µm), with a statistically significant difference across groups ($p < 0.001$).

Table 2: Comparison of RNFL thickness (µm) among study groups

Quadrant	Control (n=41)	No DR (n=41)	DR (n=41)	p-value
Superior	126.5 Â± 10.2	120.4 Â± 11.1	112.7 Â± 12.6	<0.01
Inferior	128.3 Â± 9.8	122.1 Â± 10.5	115.8 Â± 11.4	<0.01
Nasal	74.6 Â± 8.5	71.2 Â± 7.9	68.3 Â± 8.2	0.07
Temporal	72.3 Â± 7.4	69.5 Â± 6.8	66.2 Â± 7.0	0.09
Global	100.4 Â± 7.8	95.7 Â± 8.1	90.9 Â± 8.5	<0.001





Correlation with Clinical Variables

RNFL thickness showed a significant negative correlation with both duration of diabetes ($r = –0.42$, $p < 0.01$) and HbA1c levels ($r = –0.31$, $p = 0.02$). This indicates that longer disease duration and poorer glycemic control are associated with greater RNFL thinning.

Regression Analysis

On multivariate regression, duration of diabetes ($\beta = –0.38$, $p = 0.001$) emerged as an independent predictor of RNFL thinning, whereas HbA1c, though elevated in diabetics, did not retain independent significance after adjustment ($p = 0.08$).

Table 3: Multivariate regression analysis for predictors of RNFL thinning

Variable	Beta (Î²)	p-value
Duration of diabetes	-0.38	0.001
HbA1c	-0.21	0.08
Age	-0.12	0.14

Our data provide evidence of a statistically significant decrease in RNFL dimensions in diabetic patients, especially those with NPDR, compared to non-diabetic controls. Photographed RNFL thinning was observed in average and quadrant RNFL measurements, thus emphasizing the neurodegenerative basis of diabetic retinal disease. These findings underscore the importance of structural retinal examination in addition to the traditional assessment of diabetic retinopathy, and they indicate that RNFL measurement may help in early detection of neurodegeneration in diabetes.

DISCUSSION

This study evaluated retinal nerve fibre layer changes in diabetic patients and explored potential clinical predictors for RNFL thinning. Our results demonstrate that diabetic patients, even without clinically apparent retinopathy, exhibit a significant reduction in RNFL thickness compared to non-diabetic controls. The thinning was most pronounced in patients with non-proliferative diabetic retinopathy. The association between RNFL thinning and duration of diabetes was particularly noteworthy.[11] Patients with longer disease duration exhibited greater structural loss, reinforcing the cumulative effect of chronic hyperglycemia on retinal neurons.[12] Although HbA1c levels were higher in diabetic groups, multivariate analysis did not establish HbA1c as an independent predictor of RNFL thinning.[13] This finding suggests that poor glycemic control contributes to disease progression, and structural retinal damage may also depend on

factors such as cumulative metabolic stress, oxidative damage, and microvascular compromise.

Our findings are consistent with previous reports highlighting early neuroretinal alterations in diabetes preceding microvascular changes.[14] Studies using optical coherence tomography have demonstrated similar RNFL and ganglion cell complex thinning in diabetics without retinopathy, pointing toward neurodegeneration as a parallel mechanism of disease progression.[15] Such structural changes may not only reflect the severity of diabetes but also serve as potential biomarkers for early detection and risk stratification.

From a clinical perspective, integrating RNFL assessment into routine diabetic eye care may offer significant value. Identifying neurodegenerative changes before the onset of retinopathy could allow for earlier interventions aimed at neuroprotection and tighter systemic control. This proactive approach may complement conventional microvascular screening strategies and improve overall visual outcomes in diabetic patients.

CONCLUSION

In this cross-sectional study, we found that RNFL thickness is significantly reduced in diabetic patients compared to non-diabetic controls, with further thinning observed in those with non-proliferative diabetic retinopathy. Duration of diabetes emerged as a strong predictor of RNFL loss, whereas HbA1c, though elevated, was not independently associated after adjustment for confounding factors. These findings highlight the importance of recognizing neurodegeneration as an integral component of diabetic retinal disease. Incorporating RNFL assessment into routine screening may facilitate earlier detection of retinal changes and support timely preventive strategies to preserve vision in diabetic patients.

Recommendations and Limitations: This study emphasizes the value of optical coherence tomography-based RNFL measurements as a potential tool for early screening of diabetic retinal neurodegeneration. We recommend integrating RNFL assessment into routine diabetic eye evaluations, especially for patients with longer disease duration, to identify subtle neurodegenerative changes before the onset of overt retinopathy. Future longitudinal studies with larger, multi-centric cohorts are warranted to confirm these findings and explore the predictive value of RNFL thinning in progression to sight-threatening diabetic retinopathy.

However, certain limitations should be acknowledged. Being a cross-sectional, hospital-based study, causal inferences could not be established. The relatively small sample size may limit generalizability, and excluding proliferative diabetic retinopathy patients restricts understanding of RNFL alterations at advanced disease stages. Additionally, systemic factors such as blood pressure and lipid levels, which may influence retinal neurodegeneration, were not fully explored. Despite these limitations, the present findings provide important insights into the neurodegenerative component of diabetic retinal disease.

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