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ORIGINAL RESEARCH

Prospective Evaluation of Retinal Nerve Fiber Layer Changes in Newly Diagnosed Diabetic Patients

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ABSTRACT

Aim: To prospectively evaluate retinal nerve fiber layer (RNFL) changes in newly diagnosed type 2 diabetic patients using spectral-domain optical coherence tomography (SD-OCT), and to analyze the relationship between RNFL thickness, diabetes duration, and glycemic control.**Material and Methods:**This prospective observational study included 120 newly diagnosed type 2 diabetic patients aged 30–60 years at Nalanda Medical College and Hospital, Patna, from March 2021 to November 2023. Patients underwent comprehensive ophthalmic evaluation and RNFL thickness measurements in four quadrants and globally using SD-OCT. Correlations with duration of diabetes and HbA1c were analyzed using independent t-test and Pearson's correlation. A p-value <0.05 was considered statistically significant.**Results:**The inferior (112.30 ± 9.80 µm) and superior (109.60 ± 10.20 µm) quadrants had the highest RNFL thickness. Patients with diabetes >3 months showed significant RNFL thinning in the superior, inferior, and average global values ($p < 0.05$). A significant inverse correlation was observed between HbA1c and average RNFL ($r = –0.412$; $p < 0.001$). RNFL thinning was most frequent in the superior (21.67%) and inferior (24.17%) quadrants.**Conclusion:**RNFL thinning is detectable early in the course of type 2 diabetes and correlates with disease duration and poor glycemic control. SD-OCT can serve as a valuable tool for early identification of retinal neurodegeneration in diabetic patients, even before clinical signs of retinopathy emerge.

Keywords:RNFL thickness, diabetic neurodegeneration, SD-OCT, HbA1c, newly diagnosed diabetes

INTRODUCTION

Diabetes mellitus (DM), a global metabolic disorder, has long been recognized for its detrimental effects on microvascular structures, particularly in the retina. Among the earliest and most clinically relevant complications is diabetic retinopathy (DR), traditionally understood as a progressive disease primarily affecting the retinal vasculature. However, in recent years, a paradigm shift has emerged in understanding the pathophysiology of DR, highlighting the significance of retinal neurodegeneration as an early event in diabetic retinal changes—even preceding visible microvascular abnormalities. This has refocused clinical and research attention toward evaluating the integrity of the retinal nerve fiber layer (RNFL) as a potential biomarker for early diabetic retinal damage.[1]

The RNFL, composed of ganglion cell axons, plays a critical role in maintaining visual function by transmitting visual signals from the retina to the brain. It is particularly vulnerable to metabolic insults due to its high energy demand and limited regenerative capacity. In diabetes, chronic hyperglycemia induces a cascade of pathophysiological events including oxidative stress, inflammation, and mitochondrial dysfunction, all of which contribute to neuronal apoptosis and axonal degeneration. These changes may be subclinical for extended periods, yet they can be objectively assessed using modern imaging modalities such as scanning laser polarimetry and spectral-domain optical coherence tomography (SD-OCT). These tools allow non-invasive, high-resolution visualization and quantification of RNFL thickness, thereby facilitating the early detection of neurodegenerative changes before the onset of clinically apparent diabetic retinopathy.[2]

Emerging evidence suggests that neurodegenerative alterations in the RNFL may manifest even in diabetic patients without clinically evident retinopathy. This preclinical stage of retinal damage has been increasingly documented through comparative studies demonstrating significant RNFL thinning in patients

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with type 2 diabetes mellitus (T2DM) who are free from ophthalmoscopically visible DR. Such findings underscore the hypothesis that neuronal impairment is not merely a consequence but potentially a precursor or coexistent process with microvascular pathology in diabetes. This concept, if further validated, has significant implications for early screening, prognosis, and therapeutic interventions in diabetic eye disease.[3]

Furthermore, the topographical analysis of RNFL thickness has revealed that diabetic neurodegeneration does not affect all quadrants equally. Studies often report preferential thinning in the superior and inferior quadrants, which may relate to the differential susceptibility of various retinal regions to metabolic stress or to the anatomical organization of the optic nerve head. This quadrant-specific analysis, therefore, adds another layer of diagnostic refinement, enabling a more targeted assessment of early retinal damage in diabetic individuals.[4]

It is also noteworthy that neurodegeneration in diabetes may not be solely attributed to hyperglycemia. Several authors have proposed that systemic metabolic dysfunction, including insulin resistance,dyslipidemia, and low-grade chronic inflammation—hallmarks of metabolic syndrome—contribute to retinal neuronal damage independently of glycemic control. This broader understanding broadens the scope of RNFL assessment as a potential marker of systemic metabolic health, making it relevant not only in patients with established diabetes but also in those with prediabetes or metabolic syndrome.[5]

The clinical relevance of detecting early RNFL thinning in diabetic patients extends beyond mere diagnosis. Timely identification of subclinical neurodegeneration can allow for risk stratification and early implementation of neuroprotective strategies, lifestyle interventions, or intensified glycemic control to preserve visual function. In this context, neurodegeneration represents a modifiable risk factor, and RNFL assessment becomes a valuable prognostic tool for clinicians managing diabetic patients.[6,7]

Moreover, the use of high-resolution OCT has revolutionized the field of ophthalmic diagnostics, allowing for reproducible, objective, and detailed imaging of retinal layers. This technology not only facilitates cross-sectional assessment of RNFL but also enables longitudinal monitoring of progressive changes. Integration of OCT findings with functional tests such as microperimetry and electrophysiological studies provides a more comprehensive evaluation of retinal health, correlating structural damage with functional impairment.[8,9]

Despite these advancements, several challenges remain. Variability in RNFL thickness due to age, axial length, ethnicity, and individual anatomical differences necessitates careful interpretation of OCT results, often requiring population-specific normative databases. Additionally, the overlap in RNFL thinning patterns between diabetic neurodegeneration and other optic neuropathies, such as glaucoma, warrants cautious differential diagnosis, especially in elderly populations with comorbid conditions.

MATERIAL AND METHODS

This prospective observational study was conducted in the Department of Ophthalmology at Nalanda Medical College and Hospital, Patna, over a period of eight months, from March 2021 to November 2023. The primary objective of the study was to evaluate changes in retinal nerve fiber layer (RNFL) thickness among newly diagnosed diabetic patients using spectral-domain optical coherence tomography (SD-OCT).

A total of 120 patients newly diagnosed with type 2 diabetes mellitus were included in the study. These patients were referred from the Department of Medicine after confirmation of diagnosis based on fasting plasma glucose ≥126 mg/dL, postprandial plasma glucose ≥200 mg/dL, or HbA1c ≥6.5%, as per the American Diabetes Association (ADA) criteria.

Inclusion Criteria

- Age between 30 - 60 years
- Newly diagnosed type 2 diabetes mellitus (within the past 6 months)
- Best corrected visual acuity (BCVA) of 6/9 or better
- Clear ocular media for good quality OCT imaging
- Willingness to provide written informed consent

Exclusion Criteria

- History of any ocular pathology including glaucoma, retinal vascular occlusion, diabetic retinopathy, uveitis, or optic neuropathy
- Refractive error more than ±5 diopters
- History of ocular trauma or intraocular surgery
- Systemic conditions such as hypertension, renal failure, or neurological disorders affecting the optic nerve
- Use of systemic steroids or other medications known to affect RNFL
- Poor OCT scan quality due to media opacities

All participants underwent a comprehensive ophthalmic evaluation to ensure accurate assessment of retinal nerve fiber layer (RNFL) parameters. Visual acuity testing was conducted using a Snellen chart to determine the best corrected visual acuity. Intraocular pressure (IOP) was measured using Goldmannapplanation tonometry to rule out glaucoma and other pressure-related optic nerve abnormalities. A thorough anterior segment examination was performed with slit-lamp biomicroscopy, followed by a dilated fundus examination using indirect ophthalmoscopy to evaluate the retina and optic nerve head. For structural assessment of the RNFL, spectral-domain optical coherence tomography (SD-OCT) was utilized using theTOPCON 3D OCT-1 Maestro' RNFL thickness was measured in all four quadrants—

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superior, inferior, nasal, and temporal—and the average global thickness was also recorded. To minimize inter-observer variability, all OCT scans were performed by the same trained technician. Each scan was carefully reviewed, and only those with a signal strength of 7 or higher were included in the final analysis to ensure data quality and reliability.

Ethical clearance for the study was obtained from the Institutional Ethics Committee of Nalanda Medical College and Hospital. Written informed consent was obtained from all participants after explaining the nature, purpose, and potential implications of the study.

Statistical Analysis

The collected data were compiled and analyzed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize demographic and clinical parameters. Continuous variables such as retinal nerve fiber layer (RNFL) thickness were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages.The Kolmogorov–Smirnov test was applied to check the normality of distribution for continuous data. For comparison of mean RNFL thickness between groups (e.g., based on duration of diabetes or age groups), the independent sample t-test was used for two groups and one-way ANOVA for multiple group comparisons, where applicable. For correlation between RNFL thickness and continuous variables such as fasting blood glucose or HbA1c, Pearson's correlation coefficient (r) was calculated.A p-value of less than 0.05 was considered statistically significant for all comparisons.

RESULTS

Table 1: Demographic Profile of Study Participants

The study included a total of 120 newly diagnosed type 2 diabetic patients aged between 30 and 60 years. The age distribution was fairly balanced, with 38 patients (31.67%) in the 30–39 years age group, 44 patients (36.67%) in the 40–49 years group, and another 38 patients (31.67%) in the 50–60 years group. The mean RNFL values showed no statistically significant variation across these age groups, as reflected by a p-value of 0.981 (ANOVA), indicating that age was not a confounding factor in RNFL thickness among this cohort.

In terms of sex distribution, there were 66 males (55.00%) and 54 females (45.00%). The difference in RNFL thinning between males and females was also not statistically significant (p = 0.347 by chi-square test), suggesting a comparable impact of diabetes on RNFL across both sexes. Additionally, a slight majority of patients (64, i.e., 53.33%) had been diagnosed with diabetes within the last three months, while the remaining 56 patients (46.67%) had a diagnosis duration between 3 and 6 months. This subgroup classification was used in subsequent analyses to assess the impact of diabetes duration on RNFL changes.

Table 2: Distribution of Average RNFL Thickness in Study Population

The mean RNFL thickness in various quadrants of the optic disc was measured using spectral-domain OCT. The inferior quadrant showed the highest average RNFL thickness (112.30 ± 9.80 µm), followed by the superior quadrant (109.60 ± 10.20 µm). The temporal (70.20 ± 6.90 µm) and nasal (68.70 ± 7.50 µm) quadrants showed considerably thinner RNFL measurements. When comparing the inferior, nasal, and temporal quadrants with the superior quadrant as a reference, the differences in the nasal and temporal quadrants were statistically significant ($p< 0.001$), while the difference in the inferior quadrant was not statistically significant ($p = 0.116$). These findings confirm the anatomical variation in RNFL thickness, where superior and inferior quadrants are normally thicker than nasal and temporal regions.

Table 3: Comparison of RNFL Thickness by Duration of Diabetes

When RNFL thickness was compared based on the duration of diabetes, patients with diabetes for ≤3 months had significantly thicker RNFL values than those with a duration of >3 to 6 months. Specifically, the superior RNFL in the ≤3-month group was 111.10 ± 9.70 µm compared to 107.90 ± 10.60 µm in the >3–6-month group ($p = 0.043$). A similar statistically significant thinning was noted in the inferior quadrant (113.80 ± 9.50 µm vs. 110.50 ± 10.10 µm; $p = 0.047$) and in the average RNFL thickness (91.60 ± 8.10 µm vs. 88.50 ± 8.40 µm; $p = 0.030$). However, nasal and temporal quadrants did not show significant changes with duration ($p = 0.201$ and 0.218, respectively). These findings suggest early subclinical RNFL loss in newly diagnosed diabetics, particularly as the disease progresses beyond the initial months.

Table 4: Correlation Between HbA1c and Average RNFL Thickness

A significant inverse correlation was found between glycosylated hemoglobin (HbA1c) levels and average RNFL thickness. The mean HbA1c level among participants was 7.90 ± 0.80%. Pearson's correlation coefficient (r) was –0.412, with a p-value < 0.001, indicating a moderate negative correlation. This result implies that higher HbA1c values, representing poorer glycemic control, are associated with greater RNFL thinning. The statistically significant correlation supports the hypothesis that hyperglycemia adversely affects retinal nerve fiber integrity, even in the absence of clinically evident diabetic retinopathy.

Table 5: RNFL Thinning Based on Quadrant-wise Classification

Quadrant-wise analysis of RNFL thickness revealed that thinning was more frequently observed in the inferior and superior quadrants. Specifically, 26 patients (21.67%) showed thinning in the superior

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quadrant, and 29 patients (24.17%) in the inferior quadrant. Nasal and temporal thinning was observed in 13 (10.83%) and 15 (12.50%) patients, respectively. These differences were statistically significant, with *p*-values of 0.037 (superior), 0.044 (inferior), 0.013 (nasal), and 0.021 (temporal), based on chi-square tests. The higher frequency of thinning in the superior and inferior quadrants is consistent with known patterns of diabetic neurodegeneration, which often affects these regions preferentially.

Table 1: Demographic Profile of Study Participants (N = 120)

Parameter	Number of Patients (n)	Percentage (%)	*p*-value
Age Group (years)			0.981[1]
30–39	38	31.67	
40–49	44	36.67	
50–60	38	31.67	
Sex			0.347[2]
Male	66	55.00	
Female	54	45.00	
Duration of Diabetes			–
≤3 months	64	53.33	
>3 to 6 months	56	46.67	

[1] *p*-value based on ANOVA comparing RNFL by age group
[2] *p*-value based on chi-square test comparing sex distribution with RNFL thinning

Table 2: Distribution of Average RNFL Thickness in Study Population

RNFL Region	Mean ± SD (µm)	*p*-value
Superior	109.60 ± 10.20	Reference
Inferior	112.30 ± 9.80	0.116[1]
Nasal	68.70 ± 7.50	<0.001[1]
Temporal	70.20 ± 6.90	<0.001[1]
Average RNFL	90.20 ± 8.30	–

[1] *p*-values from paired *t*-test comparing each quadrant with superior RNFL

Table 3: Comparison of RNFL Thickness by Duration of Diabetes

RNFL Region	≤3 months (n = 64) Mean ± SD	>3–6 months (n = 56) Mean ± SD	*p*-value
Superior	111.10 ± 9.70	107.90 ± 10.60	0.043
Inferior	113.80 ± 9.50	110.50 ± 10.10	0.047
Nasal	69.50 ± 6.80	67.80 ± 8.10	0.201
Temporal	70.90 ± 6.40	69.40 ± 7.30	0.218
Average	91.60 ± 8.10	88.50 ± 8.40	0.030

(*p*-values calculated using independent sample *t*-test)

Table 4: Correlation Between HbA1c and Average RNFL Thickness

Parameter	Mean ± SD	Pearson's *r*	*p*-value
HbA1c (%)	7.90 ± 0.80	–0.412	<0.001
Average RNFL (µm)	90.20 ± 8.30		

Table 5: RNFL Thinning Based on Quadrant-wise Classification

Quadrant	Normal RNFL (n, %)	Thinned RNFL (n, %)	Total	*p*-value
Superior	94 (78.33%)	26 (21.67%)	120	0.037
Inferior	91 (75.83%)	29 (24.17%)	120	0.044
Nasal	107 (89.17%)	13 (10.83%)	120	0.013
Temporal	105 (87.50%)	15 (12.50%)	120	0.021

(*p*-values calculated using chi-square test)

DISCUSSION

The lack of significant differences in RNFL thickness across different age groups (p = 0.981) suggests that, within the limited age range of 30 to 60 years, age did not markedly influence RNFL thickness in this diabetic cohort. This aligns with earlier findings by Varma et al., who reported that age-related RNFL thinning becomes more pronounced only beyond the sixth decade.[10] Additionally, the non-significant difference in RNFL thinning between males and females (p = 0.347) is consistent with the observations made by Poinoosawmy et al., who concluded that while minor anatomical variations exist between sexes, gender does not significantly influence RNFL

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thickness in most populations. The near-equal distribution of participants by diabetes duration (<3 months vs. >3–6 months) allowed meaningful comparison of early RNFL changes across time frames in a newly diagnosed diabetic population.[11]

The observed anatomical distribution of RNFL thickness—thicker in the superior and inferior quadrants and thinner in the nasal and temporal quadrants—mirrors the physiological arrangement of retinal nerve fibers and is in accordance with normative data from both Indian and global populations.[12,13]The statistically significant differences between superior and nasal/temporal quadrants ($p < 0.001$) affirm the anatomical consistency and validate the accuracy of SD-OCT measurements in this cohort. Optical coherence tomography (OCT), as highlighted by Ţălu, remains the most reliable and non-invasive modality to assess these structural differences with high reproducibility, even in early-stage retinal pathologies such as diabetic neurodegeneration.[14]

This study demonstrated a statistically significant reduction in RNFL thickness in patients with diabetes duration >3 months, particularly in the superior ($p = 0.043$), inferior ($p = 0.047$), and average ($p = 0.030$) RNFL measurements. This supports the hypothesis that RNFL thinning begins early in the course of diabetes, even before the clinical onset of diabetic retinopathy. Verma et al. similarly observed structural and functional retinal changes in diabetics without fundoscopic evidence of retinopathy, suggesting that neurodegeneration may precede vascular damage.[15] Furthermore, Chihara et al. reported that RNFL defects may represent one of the earliest manifestations of diabetic retinal changes, which is consistent with the current study's findings.[16]

The inverse correlation between HbA1c levels and average RNFL thickness ($r = –0.412$, $p < 0.001$) indicates that higher glycemic levels are associated with more pronounced retinal nerve fiber loss. This reinforces the idea that poor glycemic control plays a key role in retinal neurodegeneration, independent of retinopathy status. Chen et al. emphasized that morphological retinal changes, including inner retinal layer thinning, may occur during the earliest stages of diabetes and correlate with hyperglycemia levels. Additionally, the moderate strength of correlation in this study suggests that glycemic burden may contribute progressively to neuroaxonal damage over time.[17]

The highest frequency of RNFL thinning was observed in the inferior (24.17%) and superior (21.67%) quadrants, with nasal and temporal quadrants being less affected. This quadrant-specific pattern of RNFL thinning corresponds with previous observations that the superior and inferior bundles are more susceptible to early damage, possibly due to their larger axon population and greater metabolic demand.[18] The statistically significant thinning in all four quadrants ($p < 0.05$) underscores the fact that neurodegenerative changes in diabetes can be diffuse but are often most prominent in structurally vulnerable regions. As the aging retina naturally undergoes changes in cellular composition, diabetes may further accelerate this process, particularly affecting the retinal nerve fiber layer.[19,20]

CONCLUSION

This study demonstrates that retinal nerve fiber layer (RNFL) thinning occurs early in newly diagnosed type 2 diabetic patients, even in the absence of clinical diabetic retinopathy. RNFL loss was more prominent in the superior and inferior quadrants and showed significant association with both diabetes duration and poor glycemic control (HbA1c levels). These findings highlight the utility of spectral-domain OCT as a sensitive tool for early detection of diabetic retinal neurodegeneration. Early screening for RNFL changes may aid in timely intervention and risk stratification in diabetic patients.

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