

RETINAL NERVE FIBER LAYER THICKNESS IN NORMAL SUBJECTS AND PRIMARY OPEN ANGLE GLAUCOMA.

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KEYWORDS

RNFL THICKNESS, SD-OCT, POAG,VISUAL FIELDS.

ABSTRACT

PURPOSE- To study the thickness of retinal nerve fiber layer in cases of primary open angle glaucoma and compare it with normal population of same age group using Spectral Domain Optical Coherence Tomography (SD-OCT).

MATERIALS AND METHODS – The peripapillary retinal nerve fiber layer thickness 360° and the four-quadrant average RNFL thickness (superior, nasal, inferior, and temporal) were quantitatively measured using SD-OCT in a prospective observational and case control research. Over the course of a year, the research was carried out at the tertiary eye care hospital's glaucoma department. The research comprised 60 eyes from 30 patients with POAG between the ages of 40 and 65 as well as age- and gender-matched 60 eyes from 30 healthy volunteers. Exclusions from the research included patients with significant media opacity, retinal disease, and intraocular surgery histories. Patients enrolled in the research gave their informed permission. Slit lamp, Snellen's chart, Applanation tonometer, Gonioscope, and 90 D slit lamp biomicroscope were used to analyze each one in order to research Fundus oculi. Three groups of glaucomatous eyes were separated based on visual field abnormalities. Additionally, RNFL thickness and MD correlation was carried out.

Results - In participants with control, early glaucoma, moderate glaucoma, and severe glaucoma, the average RNFL thickness was 88.8+/- 7.31, 61.68 ±10.66, 61.43 ±12.43, and 52.88±5.72 µm, respectively. Between the normal and all glaucoma categories, there was a significant difference in all RNFL thickness measurements (P<0.001). In glaucoma-affected eyes, the mean deviation demonstrated a significant connection (P<0.02) with RNFL thickness.

Conclusion: Even in the early stages of glaucoma, RNFL thickness may be a helpful adjunct in objectively and quantitatively differentiating between glaucomatous and normal eyes. It may also aid to discriminate between different severities of glaucoma. OCT can be used to identify early glaucoma and monitor glaucomatous progression to slow down further vision loss.

INTRODUCTION-

The main public health concern is glaucoma, which is the primary cause of permanent vision loss globally¹. According to data from the World Health Organization, glaucoma causes blindness in 5.1 million people worldwide, or 13.5% of all blindness cases. Three quarters (74%) of all instances of glaucoma are of POAG, the most frequent form of glaucoma. In wealthy countries, 50% of glaucoma patients are unaware that they have the condition; in poorer countries with limited access to healthcare, this number jumps to 90%.²

Perimetric parameters are widely used to establish the severity of glaucoma³, but objective method to assess the glaucomatous damage is necessary as SAP may not be feasible option in later stage of disease. It has been shown that damage of RNFL precedes VF loss⁴. It has been estimated that 30-50% of fibers may be lost before a visual field defect is detectable with white – on-white perimetry⁵. As a result, RNFL evaluation has become a crucial factor in the preperimetric diagnosis of glaucoma, which might help doctors identify the condition early and accurately.

The sensitivity and repeatability of current diagnostic methods, such as stereo fundus photography and tools for retinal and optic nerve head studies, are lacking.⁶⁻¹⁰ A non-invasive, non-contact technique called optical coherence tomography (OCT) enables cross-sectional in vivo imaging of the intraretinal layers¹¹. It is possible to photograph the retina's anatomic layers and quantify the thickness of the retina's retinal nerve fiber layer (RNFL) using the various reflectance characteristics of the layers¹¹⁻¹³. To assess the RFL thickness in normal eyes with varying stages of POAG, we performed a comparison investigation.

The aim of this work is to use SD-OCT to objectively evaluate and compare the thickness of the retinal nerve fiber layer in normal people to that of patients with POAG.

MATERIALS AND METHODS: A prospective, observational, and case-control research was conducted with 60 eyes from 30 healthy volunteers and 60 eyes from 30 POAG patients. A one-year study was conducted in the glaucoma department of a tertiary care eye hospital (October 2018 to September 2019). Before putting any cases or controls through the necessary investigations, an informed consent was obtained. After obtaining a thorough medical history, the subjects underwent a comprehensive ophthalmic examination that included dilated fundus examination with 90 D, Slit lamp biomicroscopy, refraction, best corrected visual acuity

(BCVA) using a Snellen chart, gonioscopy using Sussman goniolens, and indirect ophthalmoscopy. Those without glaucoma symptoms, a family history of the condition, no ocular diseases, and no ocular surgery were considered healthy participants. IOP of more than 22 mmHg on more than two occasions and glaucomatous optic neuropathy with glaucomatous field loss and optic nerve damage were indicators of glaucomatous eyes. Excluded from the research were patients with closed angle and secondary glaucomas, patients with significant media opacity or any other retinal disease, patients who received intraocular surgery, patients who experienced ocular trauma, and patients who did not grant permission.

A group of three or more neighboring points on a pattern deviation plot that have a chance of appearing in one hemifield in less than 5% of the normal population ($P < 5\%$) and one or more points that have a chance of occurring in less than 1% of the normal population ($P < 1\%$) and GHT outside of normal limits was defined as glaucomatous visual field loss. A minimum of two dependable visual field exams were necessary for the subjects, with the trustworthy exams being those with $< 33\%$ false negatives and false positives and $< 20\%$ fixation losses.¹⁴ Based on the MD index of visual fields, Hodapp-Parrish-Anderson's classification of glaucoma was used to divide the condition into three subgroups¹⁵. A visual field loss with an MD of less than -6 dB, a moderate glaucoma with an MD of between -6 and -12 dB, and a severe glaucomatous loss with an MD more than -12 dB were considered early glaucoma.

OCT was carried out using an optic disc cube 200x200 protocol and a Cirrus HD-OCT system (Carl Zeiss Meditec, Cirrus HD-OCT 5000-2408 softversion 6.5.0.772). Through the acquisition of a set of 128 horizontal scan lines made up of 512 A-scans, the scan protocol creates a 6mm x 6mm data cube. One operator obtained all of the photos. To ensure an OCT picture with an even radius of 1.73 mm around the optic nerve head (ONH), a circular scan with a circle diameter of 3.4 mm was centered around the disc. An automatic software method that detects scan signal intensity > 6 shows accurate demarcation of the anterior and posterior boundaries of the retinal layers and ONH, along with a continuous scan pattern free of picture artifacts.

Statistical Analysis

P values less than 0.05 were considered statistically significant. An ANOVA test was employed to assess for statistical significance.

RESULTS-

A total of 60 cases and controls (120 eyes) are enrolled in the study, out of which 30 POAG patients (60 eyes) are compared with age and gender matched 30 normal subjects (60 eyes). Their ages ranged from 40-65 years, with 24 females and 36 males. Of the patients with POAG, eight eyes had severe glaucomatous damage, 14 eyes had moderate damage, and 38 eyes had early damage. Table 1 displays the RNFL parameters that were calculated for the glaucoma and

control groups. The mean RNFL for control eyes, early, moderate, and severe glaucoma eyes, and 61.68 ± 10.66 , 61.43 ± 12.43 , and 52.88 ± 5.72 μm , respectively, were recorded. Based on ANOVA analysis, there was a significant difference ($P < 0.001$) in all RNFL characteristics between the control eyes and the eyes in the four glaucoma groups.

TABLE-1 OCT Measurements of Peripapillary RNFL Thickness in Normal Eyes and the Different Glaucoma Subgroups

RNFL THICKNESS(μm)	NORMAL N=60 EYES	EARLY GLAUCOMA N=38 EYES	MODERATE GLAUCOMA N=14 EYES	SEVERE GLAUCOMA N=8 EYES	P VALUE(ANOVA)
AVERAGE	88.8 \pm 7.31	61.68 \pm 10.66	61.43 \pm 12.43	52.88 \pm 5.72	<0.001
INFERIOR	114.4 \pm 17.49	70.5 \pm 18.22	62.71 \pm 13.25	51 \pm 3.30	<0.001
SUPERIOR	110.88 \pm 11.37	74.13 \pm 16.65	76.86 \pm 19.60	58.14 \pm 6.51	<0.001
NASAL	70.75 \pm 8.84	54.87 \pm 9.34	55.43 \pm 10.83	51.25 \pm 5.85	<0.001
TEMPORAL	57.38 \pm 10.35	47.92 \pm 9.64	52.86 \pm 11.08	47.88 \pm 8.18	<0.001

The mean and standard deviation of Mean Deviation of Visual fields (MD) for early, moderate, severe glaucoma and control eyes were -3.1 ± 2.29 , -9.50 ± 1.41 , -21.99 ± 7.13 and $+0.05 \pm 1.53$ Decibels(dB) respectively. The mean and standard deviation of Pattern standard deviation of Visual fields (PSD) for early, moderate, severe glaucoma and control eyes were 3.32 ± 2.04 , 8.43 ± 3.29 , 9.51 ± 3.79 and 1.39 ± 0.27 Decibels(dB) respectively. Visual field indices (MD and PSD) parameters computed in the control and glaucoma groups are presented in Table 2. Average RNFL thickness and the MD on Humphrey field analysis were shown to be significantly positively correlated ($P < 0.02$). Based on an ANOVA analysis, there was a significant difference ($P < 0.001$) in the visual field indices between the control eyes and the eyes in the different glaucoma groups. In Figure 1, the scatter plot shows a positive connection between the mean deviation in decibels and the thickness of the RNFL (μm) in POAG eyes.

TABLE 2 Comparison of MD & PSD in Decibels On Visual Fields in Normal Eyes and the Various Glaucoma Subgroups

Visual field indices	Normal eyes N=60 eyes	Early glaucoma n=38 eyes	Moderate glaucoma n=14 eyes	Severe glaucoma n=8 eyes	P value (ANOVA)
Mean deviation (MD) in decibels	+0.05±1.53	-3.1±2.29	-9.50±1.41	-21.99±7.13	$P < 0.001$
Pattern standard deviation (PSD)	1.39±0.27	3.32±2.04	8.43±3.29	9.51±3.79	$P < 0.001$

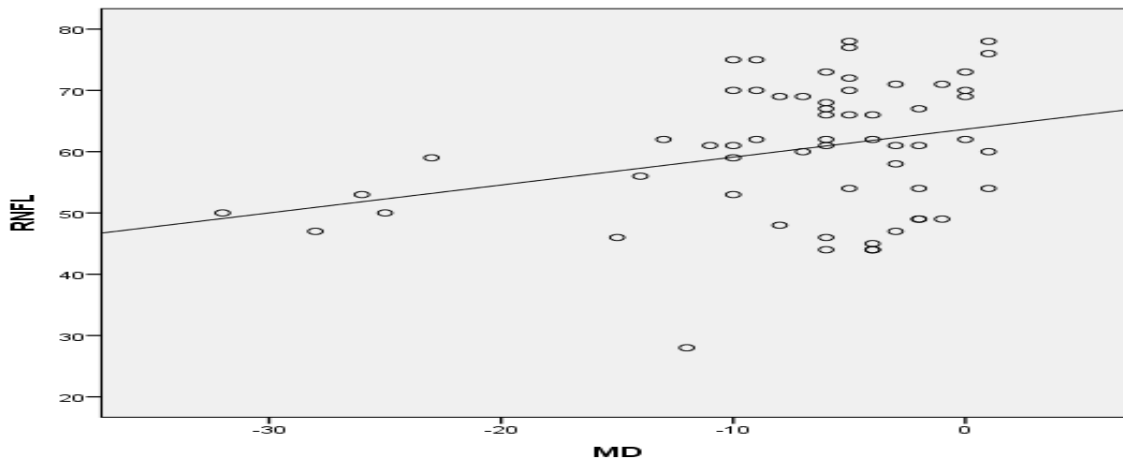


Figure 1- Mean deviation (MD) in decibels and RNFL thickness (μm) have a positive link, as shown by the scatter figure (Pearson's correlation coefficient $R = 0.301$; R^2 value is 0.091; $Y = 0.455X + 63.66$ and sig.2 tailed P value is 0.02 - statistically significant).

DISCUSSION-

The present study has been undertaken with the objective to quantitatively assess the RNFL thickness in POAG cases and to evaluate the ability of SD-OCT to distinguish normal eyes from glaucomatous eyes. We aimed to evaluate and compare the RNFL thickness in differing grades of POAG cases with age and gender matched Normal subjects. Our data was analyzed on the basis of afore described methodology.

The average thickness of the RNFL in the nasal, superior, inferior, and temporal quadrants, as well as in the peripapillary area, may be measured using RNFL-OCT, a non-invasive, non-contact diagnostic method. In glaucomatous eyes, RNFL thickness as assessed by OCT is markedly decreased, with interindividual heterogeneity.^{16,17}

In our normal group of 30 healthy volunteers (60 eyes), The lower quadrant had the thickest mean RNFL thickness, followed by the superior quadrant. The RNFL thickness in the nasal and temporal quadrants was much smaller, exhibiting a "double hump pattern"¹⁸. Similar observations were made in histological study done by **Varma and colleagues**¹⁹. The average RNFL thickness in eyes with early, moderate, severe glaucoma and in control eyes were 61.68 ± 10.66 , 61.43 ± 12.43 , 52.88 ± 5.72 and 88.80 ± 7.31 μm respectively. Similar findings of average RNFL thickness were reported by **Sihota et al**²⁰.

In our study, average RNFL thickness of 38 eyes of early glaucoma was found to be 61.68 ± 10.66 μm with mean deviation of -3.10 ± 2.29 . **Nouri Mahdavi et al**, **Kanamori et al** and **Bowd et al** also reported similar findings^{21,22,23}. Examining the Pearson's correlation between mean deviation (MD) in decibels (dB) and average RNFL thickness in POAG patients, we found a significant positive association with MD ($r=0.301$, $P=0.02$) on standard white on white perimetry (24-2 Protocol). This is comparable to Parisi et al²⁴ significant positive correlation ($r=0.393$, $P=0.03$). Highly significant positive correlation has been reported by **Sihota et al**²⁰, **Soliman et al**²⁵ and **Zangwill et al**²⁶ with $r=0.626$ ($P=0.001$), $r=0.557$ ($P=0.001$) and $r=0.660$ ($P=0.001$) respectively. The data acquired from SD-OCT offers a good objective evaluation of RNFL thickness with high reproducibility and should be correlated with clinical findings of glaucoma²⁷.

CONCLUSION:

OCT offers quantifiable, objective assessments of the extent of glaucomatous damage, which may be used to supplement perimetry findings and clinical observations. OCT is a valuable technique for tracking the development of glaucoma and for making early diagnoses. In summary, we discovered a strong association between functional alterations on visual field indices, which support findings from previous research, and the structural changes on OCT, shown as RNFL thinning in three subgroups with glaucoma.

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