

## Analysis of Retinal Nerve Fiber Layer in HIV - positive patient Using OCT at tertiary care centre

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**How to citation this article:** Dr. Kunjan Patel, Dr. Vijay Hadiyal, Dr. Harsh Gandhi, Dr. Atharva Shelar, Dr. Trupti M. Solu, “Analysis of Retinal Nerve Fiber Layer in HIV - positive patient Using OCT at tertiary care centre”, IJMACR- February - 2023, Volume – 6, Issue - 1, P. No. 521 – 525.

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**Type of Publication:** Original Research Article

**Conflicts of Interest:** Nil

### Abstract

**Purpose:** To document the Retinal Nerve Fibre Layer (RNFL) thickness in patient with Human Immune deficiency Virus (HIV) disease and to document the association between Retinal Nerve Fibre Layer (RNFL) thickness and CD4 + count.

**Design:** Cross Sectional Study.

**Methods:** The study included 104 eyes of 52 HIV Positive patients above 18 years of age with CD4+ counts above 200 were evaluated. Thickness of RNFL along a 3.4-mm-diameter circle centred on the optic nerve head was evaluated using third-generation optical coherence tomography.

**Results:** The mean age of the patients was  $39.20 \pm 10.8$  years. The mean CD4+ count in the study population was  $494.44 \pm 175.69$  cells/ $\mu$ L. Overall average RNFL thickness was  $103.48 \pm 11.69$  in right eye and  $103.23 \pm$

$10.22$  in left eye. The average RNFL thickness according to retinal quadrants in both eyes were as follows: In Superior quadrant  $123.15 \pm 22.97$  in right eye and  $128.03 \pm 18.75$  in left eye, in Inferior quadrant  $132.71 \pm 19.88$  in right eye and  $129.73 \pm 18.14$  in left eye, in nasal quadrant  $80.51 \pm 14.23$  in right eye and  $82.86 \pm 16.23$  in left eye and in temporal quadrant  $70.23 \pm 9.28$  in right eye and  $69.05 \pm 10.04$  in left eye. The average RNFL thickness in Superior quadrant  $125.59 \pm 21.11$ , Inferior quadrant  $131.22 \pm 19.09$ , nasal quadrant  $81.69 \pm 15.31$  and temporal quadrant  $69.64 \pm 9.69$ .

**Conclusion:** There was no significant change in RNFL thickness in HIV positive patients with CD4+ counts  $>200$  cells/ $\mu$ L as compared to non-HIV individuals. There was no significant correlation between CD4 + count and RNFL thickness in all the retinal quadrants.

**Keywords:** CD4+ Counts, HIV, RNFL, OCT

## **Introduction**

Human immunodeficiency virus (HIV) is a member of the family Retroviridae, a group of RNA viruses that possess an RNA dependent DNA polymerase known as reverse transcriptase<sup>1</sup>. A large variety of ocular complications can arise in patients with HIV/AIDS including retinal micro vasculopathy, vascular occlusions and opportunistic infections such as cytomegalovirus (CMV) retinitis, progressive outer retinal necrosis, ocular tuberculosis and syphilis. With the introduction of highly active anti-retroviral therapy (HAART), which combine the use three antiretroviral drugs including a protease inhibitor, the incidence of ocular opportunistic infections has reduced substantially in the past decade<sup>2-7</sup>. Third-generation OCT would allow documentation and quantification of inner retinal loss in HIV patients without CMV retinitis and would allow longitudinal studies and determination of associated risk or causative factors of retinal damage in this population and useful in diagnosis of early subclinical HIV-associated visual functional loss<sup>8</sup>. The newer protocols to assess the optic nerve head (ONH) and retina include the ONH analysis and RNFL thickness analysis along 3.4 mm diameter circle around the disc<sup>9</sup>. The present study aims to investigate the OCT characteristics of RNFL thickness in patients with HIV. We plan to evaluate the possibility of structural RNFL changes using optical coherence tomography as the imaging modality.

## **Material and method**

The study was conducted in the Ophthalmology Department at a tertiary care hospital. Permission to conduct the study was obtained from Human Research and Ethics Committee (HREC) and Anti-Retroviral (ART) Centre of the tertiary care hospital of South

Gujarat and Gujarat state AIDS control society (GSACS). HIV Positive patients referred from ART Centre to Ophthalmology OPD for any vision related problem who fulfilled the inclusion criteria were evaluated by a pair of Consultant and a Resident doctor. Patients who gave consent to Participate in the study above 18 years of age who are receiving treatment from ART Centre and CD4+ count >200. Participants were informed about the study and following which an informed consent of the patients was taken for participation in the study. Patients who have been diagnosed with infectious eye lesions such as herpes virus related eye diseases (pure herpes simplex viral keratitis, acute retinal necrosis, etc.) pneumocystis carinii choroidopathy, ocular toxoplasmosis, bacterial and mycobacterium retinitis, cryptococcus optic nerve retinitis, syphilis related optic nerve retinitis, maculopathy that may affect the retina and OCT measurements, CD4+ count <200, diagnosed case of glaucoma, hypertension and diabetes, previous history of ocular trauma and trauma related surgery, any media opacity that preclude OCT examination, patients with Tuberculosis (TB) & on Anti-Koch's treatment (AKT) and patients with HIV disease along with cytomegalovirus retinitis (CMVR) were excluded from the study. Detailed history was taken. Then the patient had undergone a series of tests and ophthalmic evaluation which included visual acuity assessment for distant vision with Snellen's illumination chart, slit lamp examination for anterior segment evaluation to rule out any ocular pathology, Intraocular Pressure (IOP) measurement was done by Non-Contact Tonometer (NCT) to rule out glaucoma followed by dilated fundus evaluation done by indirect ophthalmoscope to evaluate Posterior Segment and to rule out any pre-existing ocular

pathology that may interfere with the outcome of the study. Spectral Domain Optical Coherence Tomography (SD-OCT) using TOPCON 3D OCT-1 Maestro was performed on these patients after detailed history and ophthalmic evaluation. Circum-papillary RNFL thickness over temporal-superior-nasal-inferior-temporal circle placed automatically over the optic disc Centre was recorded in 4 quadrants and 12 clock-hour sectors around the TSINT circle. The data was collected with predesigned proforma and entered in Microsoft Excel and analysed by using SPSS version 26. Measures of central tendency (mean, median, standard deviation) were used for quantitative variables. Pearson Correlation was applied to find correlation between RNFL thickness and CD4+ counts. Outcome variables were displayed using different graphs and diagrams. Later, it was expressed using descriptive statistics.

## Results

Study conducted at the tertiary health care Center in which 52 HIV positive patients with CD4+ count more than 200 were evaluated. The mean age of the patients was  $39.20 \pm 10.8$  years and a majority of patients were between 30 to 39 years (42%) of age group. The male: female ratio was 1.88: 1. The mean CD4+ count in the study population was  $494.44 \pm 175.69$  cells/ $\mu$ L.

Table 1 shows overall average RNFL thickness was  $103.48 \pm 11.69$  in right eye and  $103.23 \pm 10.22$  in left eye. In the Superior quadrant, the mean RNFL thickness was  $123.15 \pm 22.97$   $\mu$ m in right eye and  $128.03 \pm 18.75$   $\mu$ m in left eye. In the Inferior quadrant, it was  $132.71 \pm 19.88$   $\mu$ m in right eye and  $129.73 \pm 18.14$   $\mu$ m in left eye. The mean RNFL thickness in the Nasal quadrants was  $80.51 \pm 14.23$   $\mu$ m in right eye and  $82.86 \pm 16.23$   $\mu$ m in left eye. Lastly, in the Temporal quadrant, it was  $70.23 \pm 9.28$   $\mu$ m in right eye and  $69.05 \pm 10.04$   $\mu$ m in

left eye. There was no significant difference in mean RNFL measurements between Right eye and Left eye.

## Discussion

Our study included the patients between the group of 20-69 years. The mean age of presentation was  $39.2 \pm 10.8$  years. Majority (42%) of patients were between 30 to 39 years of age group. Kozak et al.<sup>8</sup> in 2005 conducted a similar study which included 36 eyes of 18 HIV Positive patients with mean age of  $41.77 \pm 8.15$  years. In the present study, out of 52 participants, 34 (65%) were males and 18 (35%) were females. The sex ratio of the study was about 1.88: 1. Akmaz B et al.<sup>10</sup> in 2020 conducted a study of total 45 participants, amongst which 34 were male and 11 were female. In this study, the mean CD4+ counts were 494.44 cells/ $\mu$ L with a standard deviation of 175.69 cells/ $\mu$ L. Arantes TE et al.<sup>9</sup> in 2010 did a study in which the mean CD4+ count was  $502.29 \pm 41.36$  cells/ $\mu$ L and Akmaz B et al. 2020<sup>10</sup> in 2020 done a study in which the CD4+ count was  $605.4 \pm 279.5$  cells/ $\mu$ L.

The present study had no control group, so table 2 show comparison of RNFL thickness in HIV Positive patients of our study with the normal individuals from the similar previous studies. The present study suggests that the RNFL thickness is normal in both these groups. KOZAK et al.<sup>8</sup> in 2005 concluded that the HIV-positive patients whose CD4 cell counts never dropped to below 100 had an overall retinal nerve fiber layer (RNFL) thickness not significantly different from the HIV-negative population. Arantes TE et al.<sup>9</sup> in 2010 concluded that the HIV-positive patients with high CD4 cell counts (CD4 count >100 cells/mm<sup>3</sup>) had no significant retinal nerve fiber layer (RNFL) thickness change when compared with the non-HIV control.

Pearson Correlation was applied to find the correlation between RNFL thickness and CD4+ counts show in table 3. Our findings of the present study suggest that there is no significant correlation between CD4+ count and RNFL thickness in all the retinal quadrants as the patients with low CD4 count were not included in our study.

### Conclusions

There was no significant change in RNFL thickness in HIV positive patients with CD4+ counts >200 cells/ $\mu$ L as compared to non-HIV individuals. There was no significant correlation between CD4+ count and RNFL thickness in all the retinal quadrants.

### Acknowledgment

We acknowledge Gujarat State AIDS Control Society (GSACS) for permitting me to carry out my study. We are grateful to the staff of the ART Clinic of tertiary care hospital, Surat for their assistance during data collection.

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**Legend Tables**

Table 1: Average RNFL thickness of right and left eye according to retinal quadrants (n=52)

RNFL Thickness		Mean ± SD
Superior	Right Eye	123.15 ± 22.97
	Left Eye	128.03 ± 18.75
Inferior	Right Eye	132.71 ± 19.88
	Left Eye	129.73 ± 18.14
Nasal	Right Eye	80.51 ± 14.23
	Left Eye	82.86 ± 16.23
Temporal	Right Eye	70.23 ± 9.28
	Left Eye	69.05 ± 10.04
Overall	Right Eye	103.48 ± 11.69
	Left Eye	103.23 ± 10.22

Table 2: Comparison of RNFL thickness between HIV positive patients in present study and normal individual in previous similar study

Retinal area	Present study (HIV positive)	KOZAK et al. <sup>[15]</sup> (Normal)	Akmaz B et al. <sup>[71]</sup> (Normal)	Lamirel C et al. <sup>[77]</sup> (Normal)	Arantes TE et al. <sup>[61]</sup> (Normal)
Temporal	69.64 ± 9.69	75.89 ± 17.69	66.40 ± 8.90	68.9±11.5	71.42 ± 1.87
Superior	125.59 ± 21.11	122.69 ± 12.67	119.77 ± 12.94	123.8±14.8	129.36 ± 2.51
Nasal	81.69 ± 15.31	78.28 ± 15.09	73.88 ± 8.13	75.6±15.2	89.42 ± 3.37
Inferior	131.22 ± 19.09	137.20 ± 17.47	127.44 ± 12.43	130.2±14.5	138.57± 2.65
Overall	103.35 ± 10.98	103.33 ± 8.50	96.58 ± 7.37	99.6±8.3	107.16± 1.91

Table 3: Correlation coefficients of CD4 + count with RNFLT in different retinal quadrants (n=52)

Retinal quadrants	Average RNFLT In μm	Mean CD4+ count	Correlation coefficient	p-value
Temporal	69.64	494.44 ± 175.69	-0.149	0.128
Nasal	81.69		0.064	0.518
Superior	125.59		0.108	0.273
Inferior	131.22		-0.068	0.493
Average of all	103.35		-0.014	0.889