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Editorial Note

# Retinal Nerve Fibre Layer Thickness in Hiv Postive Patients: A Cross Sectional Study From A Tertiary Care Centre In Eastern India

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## Abstract

We analysed retinal nerve fibre layer (RNFL) thickness of 38 adults with Human Immunodeficiency Virus infection without any retinopathy on fundus examination, using Spectralis HRAOCT, after ruling out glaucoma. Mean age of the population was 36.2±8.17 years, and mean CD4 count was 325.7±159.3. Significant thinning of RNFL was noted in 47.3% patients, with predominant involvement of the temporal retina. No significant association could be found with CD4 cell count or age (p=0.22and 0.42 respectively).

**Keywords:** human immunodeficiency virus, retinopathy, retinal nerve fibre layer

## Introduction

Human Immunodeficiency Virus (HIV) is a global pandemic affecting around 36.7 million people globally, and results in almost a million deaths each year [1]. In India, the prevalence is as high as 0.26% [2].

Ocular involvement is often seen in HIV infection, the prevalence increasing with falling CD4 counts [3]. Other than opportunistic infections, subtle vision abnormalities are reported to be common in HIV infected individuals. It has been attributed to loss of cells in the nerve fibre layer (RNFL), with autopsy studies demonstrating as much as 40% reduction in the optic nerve neurons [4].

There have been many proposed mechanisms for this degenerative disorder which include direct damage of neural tissue by HIV, collateral damage from the body's immunologic response, and cumulative damage by microvascular circulatory abnormalities.

Cotton wool spots, representing infarcts of the retinal nerve fibre layer are common, seen in approximately 50-60% of patients with advanced disease and are the earliest and most consistent finding in HIV retinopathy [5].

We aim to estimate retinal nerve fibre layer (RNFL) thickness in ambulatory HIV infected individuals on anti-retroviral therapy, who do not have retinal pathology on ophthalmoscopy.

## Methodology

We enrolled 38 patients with HIV infection without any other systemic illness, after screening for retinal pathology using direct ophthalmoscopy. Glaucoma was ruled out using automated perimetry. Informed consent was taken, and data was collected regarding age, sex and CD4 cell count (per cu mm) done within last one month.

RNFL thickness was analysed using Heidelberg Engineering HRA Spectralis OCT in undilated eyes, and measured from a 3.6 mm circular area around the optic nerve head using infrared rays of wavelength 830 nm and resolution of 3 µm. In case of distortion of any image was found to be distorted, the examination was repeated.

Output data included both actual RNFLT (in microns) in the four quadrants (temporal, nasal, superior, and inferior) of the circle. Qualitative grading was given by the Heidelberg eye explorer software® inbuilt in the machine using normative Indian data for age and sex. Thinning was defined if p value was less than 0.05 as per in-built software. The data were entered in Microsoft Excel worksheet and later transferred to SPSS software version 21 (IBM Crop. 2012, IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY, USA).

Baseline categorical variables were summarized as frequency (percentage) and continuous variables were summarized in mean (SD). Comparative analysis was carried out using Chi-Square or Fisher's exact test for categorical variables and Student-t test for continuous variables. Correlation coefficient was obtained by Pearson's test. The pvalue <0.05 was considered significant.

## Results

Out of 38 patients enrolled, mean age was 36.2±8.17 years. Male:female ratio was 1:1.

Mean CD4 cell count was 325.7±159.3 per cu mm, with 9 patients having CD4 count <200 per cu mm.

RNFL thinning was found in 18 patients (47.4%), with predominant temporal side involved (77.8%).

Correlation between CD4 cell count and age with RNFL thinning was not significant (p=0.42 and p=0.22 respectively).

## Discussion

Significant RNFL thinning in HIV was first demonstrated by Plummer et al, using confocal scanning laser tomography, in 38 patients without obvious retinopathy [3].

Colas et al, in 2007, evaluated 20 HIV positive patients for RNFL thickness along 3,4 mm diameter circle centered on the optic nerve head and macular thickness using Stratus OCT (Zeiss version 4.0.2), and followed them up for 1 year along with CD4 counts and HIV viral loads. He found significant improvement in RNFL thickness with improvement in CD4 cell count and fall in HIV viral load, most prominent in the superior area of optic nerve [7].Kalyani et al, in 2012, evaluated 57 HIV positive individuals without opportunistic ocular infections, and found significant RNFL thinning associated with poor contrast sensitivity and colour vision [8].

In 2013, Kozak et al evaluated RNFL of 43 HIV positive patients without CMV retinitis against 22 age matched controls using third generation OCT. He found that RNFL was thinnest in patients with CD4<100, and advocated the use of third generation OCT for subclinical HIV related visual loss [9].

In 2013, Pathai et al used spectral domain optical coherence tomography for RNFL analysis in 225 HIV infected patients versus 203 age and sex matched controls, and found greater thickness with higher viral load. There was no relationship of RNFL thickness with CD4 cell count [10].

In 2016, Singh et al evaluated RNFL of 55 HIV positive patients at least 2 times 6 months apart after excluding retinal pathologies. He found significant progressive thinning in the average, superior and inferior quadrant RNFL ($P$ = 0.018, $P$ < 0.01, and $P$ = 0.012, respectively), and patients with nadir CD4 <200 $mm^3$ had a statistically significant thicker RNFL in the superior and temporal quadrants as compared with patients with nadir CD4 count ≥200 $mm^3$. He concluded that RNFL thickness as measured by OCT may be falsely reassuring in the setting of HIV, perhaps due to subclinical inflammation, and advised larger prospective studies to further evaluate the progression of RNFL thinning and the impact of HIV parameters [11].
In our study, a major proportion of our patients and thinning of RNFL, which was in the temporal and temporoinferior quadrants, which is attributed to pericyte loss due to ongoing microangiopathy in the retinal microvasculature.

In contrast to the previous studies we were unable to demonstrate a relationship between thinning of retinal nerve fibre layer and CD4 cell count, which may be attributed to our smaller sample size.

## Conclusion

Thinning of retinal nerve fibre layer is significant and occurs in patients with HIV infection prior to development of visible retinopathy, which can serve as an early marker of the disease. Its relationship to CD4 cell count is yet to be understood.

## Declarations

**Ethics approval:** Approval for the study was taken from the Institutional Ethics Committee

**Consent to participate:** An informed consent was taken from the participants before enrolment

**Availability of data:** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing Interests:** Nil

**Financial support used for the study, including any institutional departmental funds:** Nil

**Author's contributions:** DB and AG conceived the idea. DB and SB collected the data and wrote the first draft. DB and AG performed the statistical analysis. DB, SB and AG reviewed and revised the manuscript. Provided critical inputs and all authors approved the final manuscript.

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