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Study of retinal nerve fibre layer thickness by 3D OCT in HIV positive patients from Eastern India

Bijoy K Chakraborty[1], Rudrajit Paul[2]*, Asim K Ghosh[3], Tushar K Bandyopadhyay[2], Shyamapada Biswas[4]

1. Resident, 3. Professor, 4. Medical Officer
   Regional Institute of Ophthalmology, Medical College Kolkata
2. Assistant Professor, Department of Medicine, Medical College Kolkata 88, College Street, Kolkata- 700073, West Bengal.

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***Corresponding author:**

Email : docr89@gmail.com
Tel.: +91-9433824341

ABSTRACT

HIV infection is associated with a lot of ocular changes. Even in absence of opportunistic infections, retinal damage may occur due to primary effect of the virus on nerve cells. These neuro-retinal changes may affect visual functions of the subject. However, studies concerning retinal thickness changes in HIV infection are almost non-existent from the Indian subcontinent. We did a small cross-sectional study in Eastern India. HIV positive persons were tested for retinal nerve fibre layer (RNFL) thinning using 3D optical coherence tomography (OCT). The CD4 counts of the patients were also measured. The retinal thickness data was compared to that of normal subjects. We had a total of 27 HIV positive patients (54 eyes) and 20 controls (40 eyes). 77% of the patients belonged to 2140 year age group. Of 27 patients, 8 (29.6%) had borderline thinning of retina and 7 had severe thinning. CD4 count of those with severe thinning was lower (282±159/cmm) compared to the total group (315±177/cmm) (p=0.66). There was no gender predilection in retinal changes. Of the 15 patients with retinal changes, 7 had thinning confined to the temporal quadrant and the rest had generalized thinning. Retinal thinning is quite common in HIV infected Indian population. However, its relation with visual impairment and other neurological changes is still to be determined.

INTRODUCTION

Optical coherence tomography (OCT) is a new technique of examining the retina in ophthalmology. This is a new imaging modality where high resolution cross sectional images of the microstructure of biological systems may be delineated in a very short time [1]. This is being used in a number of medical specialities but particularly in ophthalmology, its use has led to revolutionary developments [1]. This new technology enables non-contact, non-invasive high quality images of human retina, especially the fovea and optic disc [2]. The images are much better than the best resolution ultrasonic images, although the depth of imaging is much less in OCT. OCT works on the principle of back-reflecting and backscattering of light waves from different microstructures [3].

HIV infection is one of the epidemics of the modern world. This affects all the systems in human body, including the eye. Opportunistic infections of the eye, like cytomegalovirus retinitis, are quite common in HIV infection and may lead to retinal damages. However, recently, some retinal changes have been discovered independent of any opportunistic infection [4]. These are thought to be due to primary effect of the HIV virus on the retina. Some studies have shown significant thinning of the retina in HIV infected persons, without any sign of retinal inflammation [4]. Scanning laser imaging has shown retinal thinning in HIV infection with falling CD4 counts [5]. OCT can be a very useful tool in assessing the retina in these patients.

HIV infection is an important public health problem in India. Since many of the infected persons work as drivers or labourers, ocular changes can be detrimental to their professional life. Also, retinal changes may be a harbinger of more serious complications like dementia. However, studies regarding retinal changes in HIV infection are very rare from India. One study from Greece, using OCT, found significant thinning of retinal nerve fibre layer (RNFL) around optic disc in HIV positive children [6]. However, whether that data can be extrapolated to our Indian patients is still not known.

We therefore undertook this pilot project in a sample Indian population to determine the status of RNFL in HIV infected

persons.

MATERIALS AND METHODS

We undertook this pilot project in a Tertiary care medical college of Eastern India. This particular college has a regional institute of ophthalmology as well as a referral centre for HIV infected patients. This was a hospital-based, cross-sectional, observational case-control study. The institutional ethical committee was fully informed of the study and proper approval was obtained. Each patient was informed of the study in the native tongue and informed consent was obtained prior to the testing.

The patients were first examined clinically and blood for CD4 count was obtained. Ophthalmologic examination was done, including direct and indirect retinoscopy, to exclude any retinal infection or inflammation. Patients with retinal inflammation, history of glaucoma, diabetes, hypertension, myopia, radiation to the eye, oculotoxic drug intake, cataract or those with congenital ocular diseases were excluded from the study. Also, anyone with hazy vitreous or corneal irregularity was excluded.

The study was conducted from 1st November 2012 to 31st march 2014. Adult patients coming to the HIV referral clinic were counselled and included in the study after proper screening. The healthy controls were chosen from the relatives accompanying the patients, provided they were HIV negative. Both the cases and controls were chosen by random sampling and age and sex matching was done. Anyone aged >60 years was excluded to avoid the confounding effect of age-related retinal changes.

The RNFL thickness was measured using the HRA-OCT spectralis machines (Heidelberg engineering, Germany, 2011). The software for analysis was Heidelberg Eye Explorer, supplied by the manufacturer of the machine. All subjects were tested by the same operator on the same machine. There was no need of dilating the pupils before this test. The system used infrared rays of wavelength 830 nm. A circular area of diameter 3.4 mm around the optic nerve head was analysed, depth of imaging being 180±50 µm. the angle of light rays and depth of analysis were auto-adjusted by the machine. Each result was an average of 3 consecutive readings. The RNFL was identified by the machine using an algorithm based on its reflectivity. Each eye analysis took 23 minutes. Although retinal structures up to internal limiting membrane were seen in the output image, for this study, we only measured the RNFL thickness (RNFLT). Normative Indian data were fed in to the machine before start of the study. The output data automatically categorized the retinal thickness into normal (green), borderline (yellow) or severe thinning (red)vide figure 1. This ordinal data was considered for subsequent analysis. Only images free of artefacts or distortions were used for analysis. Images had an average resolution up to 3 µm.

The data was arranged in Microsoft Excel worksheet. The data are expressed as mean± S.D. or number/percentage depending on the nature. Students' T test was used to compare significance of difference of the means. Chi square test was used for nominal data. $P<0.05$ was considered significant.

RESULTS

There were a total of 27 patients in our study. Initially 42 patients were selected for this study but some of them did not consent to the procedure and data collection was incomplete for some others. Thus 27×2=54 eyes were examined. There were 20 healthy controls (40 eyes).

The average age of the patients was 35.41±7.88 years. Table 1 shows the age-wise distribution of the study population. It is seen that almost 77% of the patients belonged to the 2140 year age group. The male: female ratio was 12:15 (figure 2). In control group, male: female ratio was 11: 9. Average CD4 count was 315±177/cmm. There were only 3 (11.1%) patients with CD4 count≤100/cmm.

Table 1. Showing the age distribution of our patients

Age group	Number	Percentage
= 20 years	1	3.7
21-30 years	7	25.9
31-40 years	14	51.9
41-50 years	3	11.1
= 51 years	2	7.4

As figure 3 shows, there was considerable thinning of retina in the study population. 8 patients (29.6%) had borderline thinning of retina and 7 patients (25.9%) had severe thinning of retinal nerve fibre layer. Thus, altogether 15 patients had some degree of retinal nerve fibre layer abnormality. The gender ratio of this group with retinal abnormalitywas 8: 7(M: F). In comparison, none of the persons in control group had retinal abnormality ($p<0.0001$ by Fisher's Exact test, 2-tailed).

The average CD4 count of patients with severe retinal thinning was lower (282±159/cmm) compared to the average CD4 counts of the total group (315±177/cmm). However, the difference was not statistically significant ($p=0.66$). Figure 4 shows the average CD4 counts in sub-groups of the study population.

Of the patients (n=7) with severe thinning of retina, 5 (71.4%) had thinning of all the quadrants. The remaining 2 had thinning of only temporal quadrants. Of 8 patients with borderline thinning, 5 (62.5%) had changes in only temporal quadrant.

DISCUSSION

In this Eastern Indian study, significant RNFL thinning in HIV positive persons was documented. The CD4 count in those with significant thinning was lower compared to others, but the difference did not reach statistical significance.

Significant degrees of retinal thinning have been found in HIV positive persons in other studies too [5, 6]. A study from USA in 2013 found significant retinal changes in HIV infection [7]. They found that not only the RNFL but also other intra-retinal structures like pigment epithelium (RPE) and photoreceptor outer segments (POS) were affected in HIV. This may result in loss of visual function and visual fields [7]. In HIV infected professionals like drivers, this impairment may mean an end to professional life. In general, visual impairment in HIV infection is an established entity [8]. It may be clinically evident or may remain silent for a long time and be detected only by specialized tests like electroretinograms [9]. In this study, we did not check visual status of the patients, but another study comparing visual acuity with retinal NFL thickness is on-going.

The exact cause of this retinal damage is still not known.

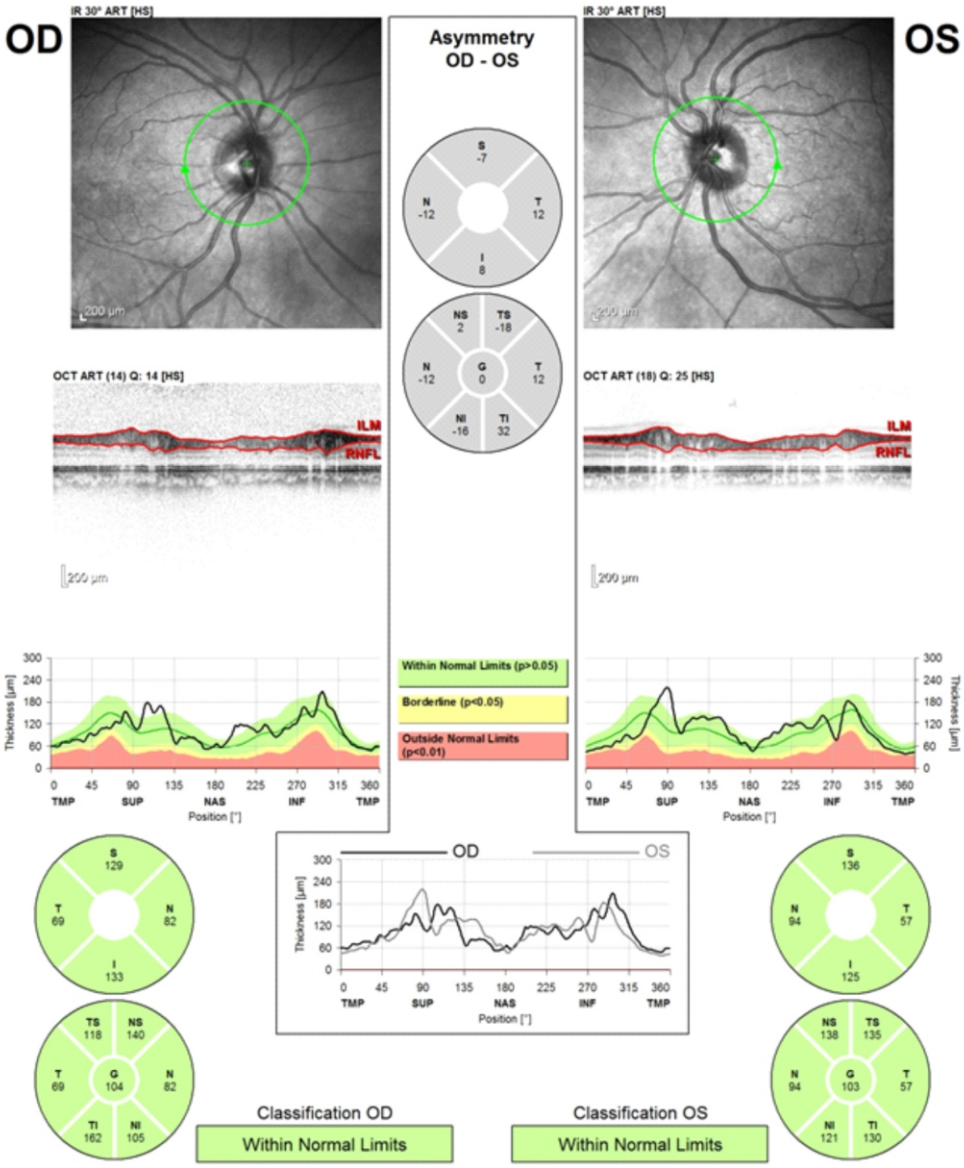

Fig 1. Showing a sample RNFLT data sheet

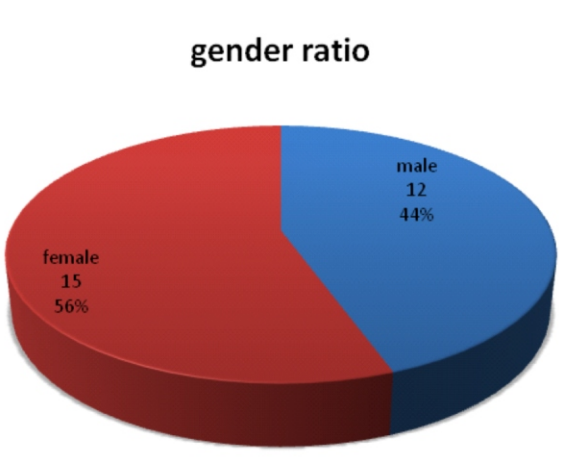

Fig 2. Showing the male: female ratio in a pie chart

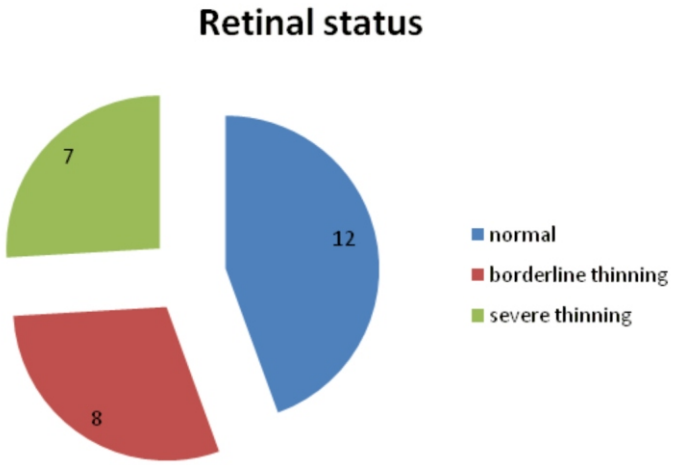

Fig 3. Pie-chart showing retinal thinning in the study population

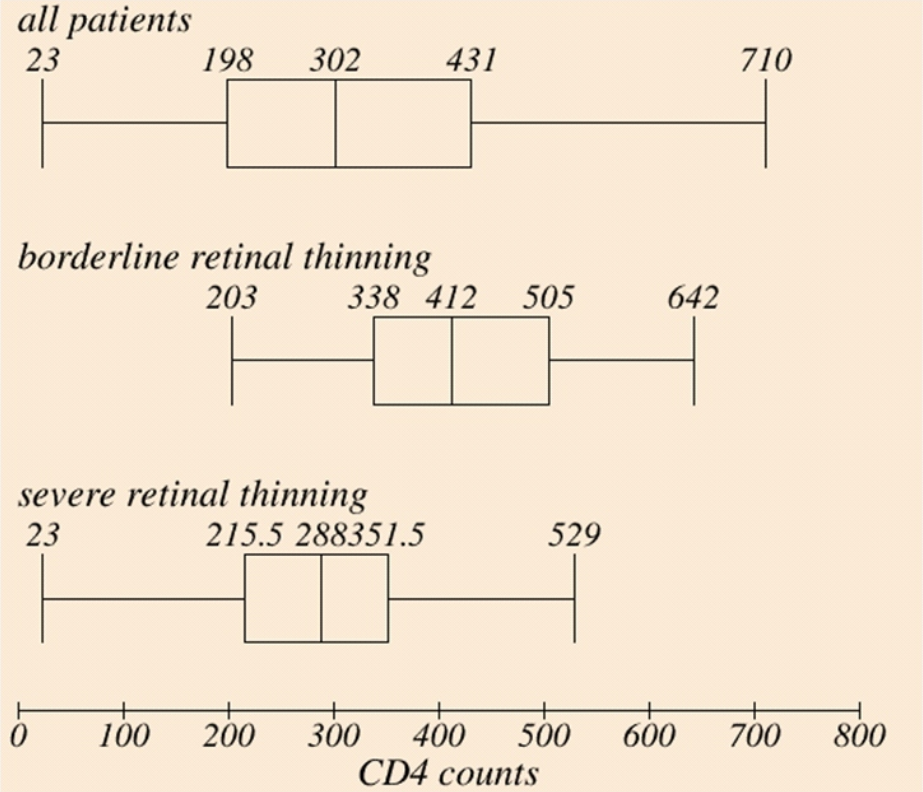

Fig 4. Box and Whisker plot showing the CD4 counts in our patients

Excluding opportunistic infections, direct or indirect effect of HIV on nerve fibres is thought to be responsible for this change [9, 10]. There are infarctions of nerve fibre layers and retinal capillary dropout [9]. This may lead to axonal loss, although the optic nerve and retina may be clinically normal. Recently, it has been shown that the gp120 protein of HIV may induce NO production in RPE cells [11]. The oxidative stress secondary to locally produced NO may be one of the pathways leading to AIDS associated retinopathy. HIV infection may also lead to cotton-wool spots and intra-retinal haemorrhages [12].

In some studies, RNFLT was found to decline with falling CD4 counts [5]. In our study, since only 3 patients had CD4<100/cmm, no conclusions can be drawn. A larger study is needed to substantiate this point. But, with improved HIV care and earlier threshold of onset of treatment, patients with low CD4 count are becoming rarer everywhere. Confocal scanning laser tomography is another method of measuring retinal thickness. Earlier, this method was widely used but now OCT is preferred [9]. This is because OCT is quicker to perform, is more reproducible and quantifiable. However, head-to-head comparison shows both the techniques to be similar in detecting retinal thinning [13]. In our set up, after the initial cost of setting up the instrument, OCT is cheaper.

We found a topographical predominance of changes in temporal quadrant of the retina. 7 out of the 15 patients with retinal changes had significant thinning of only the temporal area. This trend has also been found in other studies [9]. The retinal thinning and distribution of cotton-wool spots in retina follow similar patterns, with supero-temporal area being most affected [14].Nasal quadrant is the least affected [9]. The exact cause of this differential distribution is not known till now. The RNFL thinning is not just important from visual point of view. In some studies, this has been shown to correlate with other neurodegenerative syndromes like HIV associated dementia [15]. Thus, the spectrum of this disorder goes beyond the eye and is sometimes called HIV associated Neuroretinal disorder (HIV-NRD)[16]. The prevalence of this increases with duration of infection and is sometimes called 'accelerated ageing of HIV' [17]. Our study is probably the first of its kind from the Indian subcontinent. This clearly depicts the need for larger studies on retinal changes in HIV infection in this population

CONCLUSION

HIV infection is associated with significant retinal changes. This is a serious comorbidity for the patients and tests like OCT can detect these changes at an early stage. Thus, OCT maybe used in HIV positive individuals to detect incipient retinal damage before visual symptoms begin. Proper rehabilitative measures can then be instituted at an early stage.

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