Ocular manifestations in HIV patients and its correlation with CD4 count before and after starting HAART

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ABSTRACT

Background: Human immunodeficiency virus (HIV) infection and acquired immunodeficiency syndrome (AIDS) are a global pandemic, with cases reported from practically every country. The majority of information and studies regarding ophthalmic manifestations in India reflects the pre-HAART (highly active anti-retroviral therapy) era. India may be going through an intermediate stage, where the spectrum of the ophthalmological manifestations may be changing significantly. **Aims and Objectives:** The aims of this study were to study the age and gender distribution in HIV patients presenting with various ocular manifestation and to correlate the cluster of differentiation 4 (CD4) count with various ocular manifestation of AIDS. **Materials and Methods:** Prospective cross-sectional study was conducted on 120 patients. Ocular manifestations and WHO clinical stage of HIV were noted and CD4 count was calculated. The participants were followed up for at least 6 months on monthly basis when they come to take ART tables or as required for any ophthalmic disorder presented by patient. Any manifestation during this months was included in post HAART group. CD4 count after 6 months was taken into account in post HAART group. **Results:** Males predominated females. The number of males in Pre HAART was 60.8% and post-HAART 59.4%. Mean CD4 count in pre-HAART was 140.63 and post-HAART was 221.93. Majority (34 patients) in pre-HAART had CD4 count between 100 and 150, while in post-HAART, majority had count more than 200 (57 patients**). Conclusion:** Mean CD4 count of pre-HAART group patients raised significantly. Mean CD4 count of pre-HAART group is 140.63 with SD of 63.4, while it increased in post-HAART group to 222 which is statistically highly significant.

Key words: Cluster of differentiation 4; Highly active antiretroviral therapy; Human immunodeficiency virus; Ophthalmological

INTRODUCTION

India is emerging globally as a country with largest number of acquired immunodeficiency syndrome (AIDS) patients. Highly active antiretroviral therapy (HAART) has led to a dramatic decline in AIDS-related morbidity and mortality.[1] However, such advances in human immunodeficiency virus (HIV) therapy have not benefited those suffering from HIV/AIDS in the developing countries.[2] It was discovered in the late 1970s and was originally known as leu-3 and T4 (after the OKT4 monoclonal antibody that reacted with it) before being named cluster of differentiation 4 (CD4) in 1984.[3] CD4 is a glycoprotein expressed on the surface of T-helper cells, regulatory T-cells, monocytes, macrophages, and dendritic cells. It was discovered in the late 1970s and was originally known as leu-3 and T4 (after the OKT4 monoclonal antibody that reacted with it) before being named CD4 in 1984.[3] In humans, the CD4 protein is encoded by the CD4 gene. Ocular complications are common in HIV infected individuals.[1,2] Most studies on the prevalence of ocular complications in HIV/AIDS have been carried out in industrialized countries; nevertheless,

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more than 90% of all the patients infected with HIV live in developing countries.[4]

Aims and objectives
The aims of this study were as follows:
1. To study the age and gender distribution in HIV patients presenting with various ocular manifestation.
2. To correlate the CD4 count with various ocular manifestation of AIDS.

MATERIALS AND METHODS

Type of study
This study was prospective cross-sectional.

Sample size
The sample size was 240 eyes (120 patients)

Inclusion criteria
The following criteria were included in the study:
1. HIV positive recently diagnosed patient
2. CD4 count <250 or eligible for HAART with >250
3. Not yet started on HAART or any other antiretroviral regimens outside/private
4. Any age

Exclusion criteria
The following criteria were excluded from the study:
1. Patients having preexisting hypertensive and diabetic retinopathy.
2. Patient on anti-retroviral therapy before enrollment.
3. Old diagnosed HIV patient.
4. Default cases of HAART

Procedure
The WHO clinical stage, CD4 count, and ocular manifestations at presentation were first detected and risk factor of infection of patients was documented.

Material used was Snellens vision chart, Slit lamp, Fundoscope, Indirect ophthalmoscope, and Fundus camera.

The selected patients underwent history taking, physical examination, ocular examination, visual acuity testing and direct ophthalmoscopy, indirect ophthalmoscopy, and slit-lamp examination. Routine baseline laboratory investigations were carried out. As required fundus fluorescence ophthalmoscopy was done, B-scan, and Fundus photographs were taken.

Routine investigations including Hb, BSL, LFT, and RFT were done. The participants were followed up for at least 6 months on monthly basis when they come to take ART

tables or as required for any ophthalmic disorder presented by patient. Any manifestation during these months was included in post-HAART group. CD4 count after 6 months was taken into account in post-HAART group.

Various ocular side effects of antiretroviral drugs were noted in follow-up patients and treated accordingly. Cause of drug rash was determined as per dermatological reference and specific manifestation of that drug. Offending drug was stopped/substituted with another group. Causes of loss of follow-up were assessed from ART center records. The response to HAART was assessed in terms of a rising in the CD4 count at 6 months.

CD4 count and ocular manifestations were compared using paired t-test and Chi-square test as required.

RESULTS

In our study, we examined 240 eyes of 120 AIDS patients.

As per above table 1, males outnumbered females in both pre HAART(60.8%) and post HAART age groups(59.04%).

Table 1: Distribution of aids patients in two groups according to gender

Sex	Number of cases in pre-HAART	%	No of cases in post-HAART	%
Males	73	60.8	62	59.04
Females	47	39.2	43	40.95

Table 2: Age- and sex-wise distribution of cases

Age in years	Male	female	No. of cases	%
<10	2	0	2	1.7
10	2	2	4	3.3
20	5	17	22	18.3
30	38	15	53	44.2
40	24	6	30	25.0
50	4	5	9	7.5
Total	73	47	120	100.0

Table 3: CD4 count distribution of patients during first presentation

	N	Minimum	Maximum	Mean	SD
CD4 count	120	22	460	137.74	69.595

Table 4: Comparison of CD4 count in pre and post haart group

CD4 Count	N	Mean	Std. Deviation	Paired t	P
Pre	105	140.63	63.36	8.94	<0.001 HS
Post	105	221.93	106.60		

According to table 2, maximum cases were seen in the age group of 20-30 years(44.2%) followed by 30-40 years(25%). Males(73)dominated females(47). So, males outnumbered females.

As per table 3, maximum CD4 count noted was 460 and minimum was 22. The mean± SD was 137.74± 69.595.

As per table 4 the mean± SD for Pre- HAART and post-HAART was 140.63±63.36 and 221.93±106.60 respectively. P value was found to be statistically significant.

As per table 5, CD4 count between 100-150 was present in 34 pre HAART patients as compared to 16 post HAART patients. According to table 6, 5 cases of HIV microangiopathy, 2 cases of Herpes Zoster Ophthalmicus was found in patients with CD4 count <100.

In accordance with table 7, we have shown the comparision with the study of Sahu et al.

DISCUSSION

In the present study, the maximum age recorded was 70 years and a minimum of 2 years, out of 120 cases majority belong to age group 20–50 (87.5%) years pointing the focus of care to this group. Of all the patients, mean age of 33.4 years and age ranging from 2 to 70 years was seen.

Table 5: Range-wise distribution of CD4 count

CD4 (cells/ul)	Pre-HAART	Post-HAART
<50	10	4
50–100	32	10
100–150	34	16
150–200	19	18
>200	25	57

Table 6: Association between CD4 count and ocular manifestations at presentation

Manifestations	No.	CD4
HZO	2	<100
Molluscum Contagiosum	4	100–250
HIV Microangiopathy	5	<100
CMV Retinitis	3	<50

Table 7: Association between CD4 count and ocular manifestations at presentation

CD4 count (cells/µl)	% of patients Sahu et al.	Pre HAART %
0–50	14	8.33
51–100	21	26.66
101–150	27	28.33
151–200	38	15.83
>200	-	20.83

Of all the patients, 73 (60.8%) were male and 47 (39.2%) were female at presentation.

Sahu et al.,[5] carried that out study in western India (2008) has also reported 68% of male preponderance. However, it is in less than 90% reported in the South Indian study (1999).[6] This difference between male and female preponderance could be due to the facts like – Disease may be more prevalent in men, women may be deprived of screening modalities, men more aware of ART; illiteracy in women may be affecting them.

Still difference between south Indian study and ours may be due to-Better immunocompetence following increase in the availability and prescription of HAART in recent years, small sample size in south Indian study, and time factor, as there is more awareness in female in recent years. Both of them loudly say the male preponderance except in 20–30 groups, where there is female preponderance.

In the study, it was reported that there are 14,000 new infections in HIV occurring per day globally and 90% of them are in developing countries.[7] 12,000 out of them are in age group of 15–50 year age group which perfectly matches with age group in our study (87% in age group 20–50). Zambarakjia et al., reported the mean age of 37.28 years (SD 8.22 years) and the range was 20–77 years.[8]

Reasons of high prevalence among this age group are as follows:
- Unawareness regarding clean sexual practice.
- This comprises the earning group of society staying away from home.
- Increasing homosexuality.
- More susceptible to major trauma demanding blood transfusion.
- Intravenous drug abuse and addiction.
- Increased promiscuity in husbands is reason to make the disease prevalent in their wife in this age group.

Here in statistics, again mean CD4 count of pre-HAART group is 140.63 cells/ul with SD of 63.4 cells/ul, while it increased in post-HAART group to 222 which is statistically highly significant (P<0.001 by paired "t"-test). It proves beyond doubt that HAART is playing a major role in aids patients' life by increasing life expectancy by increasing CD4 count.

Biswas et al., reported increase of CD4 count after starting of HAART in HIV patients.[8]

All studies have shown increase in CD4 count after starting of HAART, more initially then maintaining at different level. As patients become resistant to drugs, it starts decreasing. Increase in CD4 count has led to increase in few vision threatening complications.

Majority of patients in pre-HAART group fall in the range of 100–150 cell/mm^3. However, for post-HAART group, it is in >200 cell/mm^3. That reflects the highly significant efficacy of HAART in improving CD4 count of AIDS patients.

In our study of 120 patients, follow-up was lost for 15 patients due to death due to inevitable reasons and transfer taken by patients to another ART center.

Eleven males and four females were lost to follow-up. Total deaths were ten.

Causes of death in majority of patients were tuberculosis and its complications such as
- Milliary tuberculosis: 6
- Pleural effusion: 2
- Tuberculous meningitis with secondary
- Bacterial infection: 1
- Pleural empyema with septicemia: 1

In most cases, CD4 count was below 100 indicating increased morbidity within this range.

In western India, study by Sahu et al., similarly, reported maximum patients in 150–200 groups. However, it cannot be compared to any one group directly as it contained patients with or without HAART.

In the study conducted by Sahu et al, occular manifestations were maximum in CD4 count between 101-150 followed by 51-100 CD4 count.

The mean CD4 count in study was 121.4 cells/ul, a slightly on lower side than our mean of 140.63 cells/ul with SD of 63.4 cells/uL in pre-HAART group. It may be due to now changing pattern of treatment by starting it in patients with CD4 count >200 with tuberculosis or other indications.

CD4 count was maximum in 150–200 range in other study but their inclusion criteria consisted of seropositive patients with or without HAART medications.

Limitations of the study
We could have increased the sample size and could have validated the results for whole population atleast in our area.

CONCLUSION

Mean CD4 count of pre-HAART group patients raised significantly. Mean CD4 count of pre HAART group is 140.63 with SD of 63.4, while it increased in post-HAART group to 222 which is statistically highly significant (P<0.001 by paired t-test). All ocular manifestations were more in patients with CD4 count less than 100.

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REFERENCES

1. Ali R, Kim JY and Henderson BA. Adnexal and anterior segment manifestations of HIV-AIDS. Int Ophthalmol Clin. 2007;47(2):15-32.
   https://doi.org/10.1097/IIO.0b013e318036bcc4
2. Meyer D. Eye signs that alert the clinician to a diagnosis of AIDS. SADJ. 2005;60(9):386-387.
3. Kestelyn PG and Cunningham ET Jr. HIV-AIDS and blindness. Bull World Health Organ. 2001;79(3):208-213.
4. Hodge WG, Seiff SR and Margolis TP. Ocular opportunistic infection incidences among patients who are HIV positive compared to patients who are HIV negative. Ophthalmology. 1998;105(5):895-900.
   https://doi.org/10.1016/S0161-6420(98)95033-3
5. Sahu DK, Namperumalsamy P and Walimbe P. Ocular manifestations of HIV infection/AIDS in South Indian patients. Indian J Ophthalmol. 1999;47(2):79-85.
   https://www.ijo.in/text.asp?1999/47/2/79/22797
6. Zambarakjia HJ, Newsonb RB and Mitchella SM. CMVR diagnoses and progression of CD4 cell counts and HIV viral load measurements in HIV patients on HAART. Br J Ophthalmol. 2001;85(7):837-841.
   https://doi.org/10.1136/bjo.85.7.837
7. Slogrove AL and Sohn AH. The global epidemiology of adolescents living with HIV: Time for more granular data to improve adolescent health outcomes. Curr Opin HIV AIDS. 2018;13(3):170-178.
   https://doi.org/10.1097/COH.0000000000000449
8. Biswas J, Fogla R, Gopal L, Narayana KM, Banker AS, Kumarasamy N, et al. Current approaches to diagnosis and management of ocular lesions in human immunodeficiency virus positive patients. Indian J Ophthalmol. 2002;50(2):83-96.

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SM- Concept and design of the study, prepared first draft of manuscript, Interpreted the results; **PM-** reviewed the literature and manuscript preparation; and **DB-** Concept, coordination, statistical analysis and interpretation, and revision of the manuscript.

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