

## Study of ocular manifestations in HIV positive patients at a tertiary care center in Kumaon region, Uttarakhand, India

Kalpna Kumari<sup>1</sup>, G. S. Titiyal<sup>2\*</sup>

<sup>1</sup>PG Resident, <sup>2</sup>Professor & Head, Dept. of Ophthalmology, Govt. Medical College, Haldwani, Uttarakhand

**\*Corresponding Author:**

Email: sangwankalpna@gmail.com

### Abstract

**Aims & Objectives:** To study the ocular manifestations in HIV/AIDS patients in terms of percentage of ocular involvement, pattern, relationship of ocular conditions with CD4 counts and visual deterioration by the same presenting to a tertiary care center of Kumaon region, Uttarakhand, India.

**Materials & Methods:** Hospital based observational prospective, clinical study in which 400 HIV positive patients were examined at a Tertiary care centre, Uttarakhand (Sushila Tiwari Memorial Hospital) in terms of clinical examinations, relevant investigations, treatment and were documented.

**Results:** 400 HIV positive cases were examined. The commonest systemic disease was pulmonary Tuberculosis (18%). In the study group, 28.5% of the cases had ocular involvement and, HIV retinopathy (9.2%) being the commonest HIV-associated ophthalmic lesion followed by Dry eye disorder (6.8%) & HIV microangiopathy (6.3%). Heterosexual route (89.7%) was the most common mode of transmission of disease in the patients examined. The correlation between CD4 level and ocular involvement was insignificant except in cases of HIV retinopathy (p value=0.001), HIV microangiopathy (p value=0.020) and CMV retinitis (p value=0.01).

**Conclusion:** HIV retinopathy was the most common ocular manifestation encountered in our study with mild visual deterioration and good immune status of the patient (i.e., high CD4 count). Dry eye disorder and HIV microangiopathy are the next common lesions with varied degrees of visual affection and CD4 count range. There needs to be awareness of ocular involvement among HIV infected individuals and an increased emphasis on regular ophthalmic examination in all HIV patients for timely diagnosis of the vision threatening conditions.

**Keywords:** Ocular manifestations, HIV retinopathy, CD4 count, Vision deterioration, Dry eye.

### Introduction

Human Immunodeficiency Virus (HIV) currently infects 35.3 million people across the world.<sup>(1)</sup> Overwhelming size of the Indian population makes it the country with the largest number of people living with HIV /AIDS (PLWHA). Ocular lesions attributable to HIV are seen in up to 2/3rd of the estimated 2.5 million HIV-positive population in India at some point in their lifetime.<sup>(2,3)</sup>

Ophthalmic manifestations of HIV infection are diverse. Both anterior and posterior segments of the eye can be involved and it may even lead to blindness.<sup>(4)</sup> The earliest studies on this subject stated the prevalence of ophthalmic manifestations of HIV infection ranging from 10 to 20%.<sup>(4,5)</sup> Ocular lesions in patients on highly active antiretroviral therapy (HAART) have shown changes in disease prevalence and pattern.

Ocular manifestations in HIV positive and AIDS patients range from simple Blepharitis to severe blinding conditions like CMV retinitis. In general, CD4 T-lymphocytes count has been used to predict the onset of certain ocular infections in patients who are HIV positive.<sup>(6,7)</sup> CD4 T-cell count less than 500 cells/mm<sup>3</sup> is associated with Kaposi sarcoma, lymphoma and tuberculosis. CD4 T-cell count less than 250 cells/mm<sup>3</sup> is associated with pneumocystosis and toxoplasmosis, and CD4 T-cell count less than 100 cells/mm<sup>3</sup> is associated with retinal or conjunctival

microvasculopathy, Cytomegalovirus (CMV) retinitis, varicella-zoster virus (VZV) retinitis, Mycobacterium avium complex infection, cryptococcosis, microsporidiosis, HIV encephalopathy, and progressive multifocal leukoencephalopathy.<sup>(8)</sup>

Due to the potentially devastating and rapid course of retinal opportunistic infections all persons with HIV diseases should undergo routine baseline ophthalmic evaluation. Any HIV infected person who experiences ocular symptoms also should receive prompt and competent ophthalmic care as delay in therapy can lead to irreversible visual loss.

There are not many studies on ocular lesions of HIV-positive patients, especially in hilly terrain states like Uttarakhand, India. We studied the ocular manifestations especially in terms of prevalence, pattern, correlation with CD4 T-cell count and visual deterioration caused in 400 patients with HIV registered in an ART centre functioning under a tertiary care centre in Kumaon region, Uttarakhand, India.

### Materials and Method

It was a prospective hospital based, cross-sectional observational study conducted in the Department of Ophthalmology, Government medical college, Haldwani at Sushila Tiwari Memorial Hospital from October 2014 to October 2016. 400 diagnosed cases of HIV Infection registered under ART Centre operating in Sushila Tiwari

Memorial Hospital, attending outpatient department and admitted in this hospital were randomly selected. A detailed ophthalmic examination with detailed history was carried out in all patients all the patients had CD4 T cell values at first visit. All patients irrespective of symptoms were subjected to visual acuity assessment using Snellen's chart, Schirmer's test, slit lamp examination using 90 D lens, fundus examination by indirect ophthalmoscopy with 20 D lens and tonometry with Non-contact tonometer was also carried out as required on the case basis. Results were recorded in the pre-designed proforma. Visual acuity was recorded as finger counting & hand movements in illiterate and bedridden patients. Patients on long term steroids or immune-suppressants for any systemic conditions and patients who were terminally ill / comatose or cannot be examined fully were excluded from this study.

**Ethics:** Institutional ethical clearance as well as NACO permission was taken to conduct the study. Confidentiality was maintained & no personal details of the patients were recorded after obtaining written informed consent.

**Statistics:** Data analysis was done using SPSS version 21 and descriptive interpretation of the data was done in the form of percentages. Chi-square test, Odds ratio and Binary logistic regression analysis were used as tests of significance.

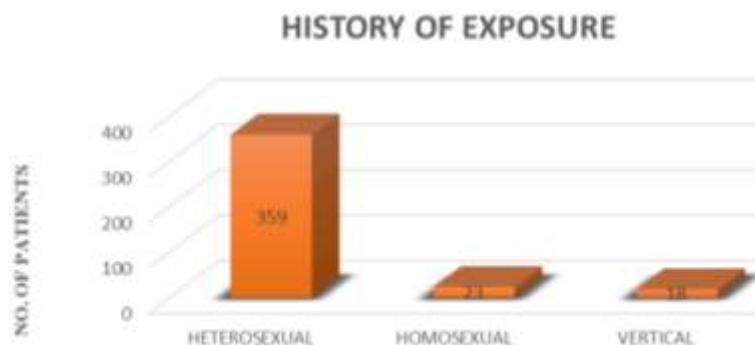
## Results

Four-hundred HIV seropositive patients were examined and 114 (28.5%) patients had ocular manifestations at the time of presentation. Age and gender distribution showed majority of the study participants (218 males and 119 female patients) were in sexually active age group of 21 to 50 years. (Table 1)

**Table 1: Age and gender distribution of patients studied**

Age group (in years)	Male	Female
0-10	5 (1.3)	4 (1)
11-20	12 (3)	8 (2)
21-30	73 (18.2)	66 (16.5)
31-40	112 (28)	53 (13.3)
41-50	33 (8.2)	27 (6.8)
51-60	5 (1.3)	1 (0.2)
61-70	1 (0.2)	0 (0)
Total	241 (60.2)	159 (39.8)

As per this study, 382 (95.5%) patients contracted infection due to sexual exposure and heterosexual route was the most common route encountered in this study. 18 (4.5%) patients had infection via perinatal route. (Fig. 1)



**Fig. 1: History of exposure**

In this study out of 400 HIV patients, 385 (96.2%) were on HAART Therapy and the remaining 15(3.8%) were not on HAART Therapy. (Fig. 2)



**Fig. 2: HAART Therapy status of patients at the time of presentation**

In the present study, ocular manifestations were seen in 114 (28.5%) patients. Many patients had multiple ocular manifestations. (Fig. 3)



**Fig. 3: Various ocular manifestations and the percentages of involvement.**

In the present study following were the ocular manifestations seen in 114 patients. 229 ocular manifestations were seen in 114 patients as many patients presented with more than 1 ocular manifestations as well as involving both anterior and

posterior segment. 37 patients (9.2%) had HIV retinopathy, which is the commonest manifestation followed by Dry eye disorder, HIV microangiopathy and Blepharitis in 27(6.8%), 25(6.3%) and 23(5.8%) patients respectively. 10 (2.5%) patients had Tubercular choroiditis, 6 patients (1.5%) had CMV Retinitis, 7 patients (1.7%) had Toxoplasma Retinochoroiditis, 5 patients (1.3%) had Herpes Zoster Ophthalmicus, 6 patients (1.5%) had Anterior Uveitis. Bell's palsy was seen in 3 patients (0.8%). Corneal opacity was seen in 5 patients (1.3%) and 24 patients (6%) had Non-specific Choroiditis. 6 patients (1.5%) had Complicated Cataract. Keratitis was seen in 6 patients (1.5%). Conjunctivitis in 22(5.5%), Molluscum Contagiosum in 12(3%), External hordeolum with 2(0.5%) patients. (Fig. 4)

Table 2 shows correlation of ocular manifestations according to CD4 counts. In this study most of the ocular manifestations were found to occur in patients having CD4 count more than 200 and relationship between ocular manifestations and CD4 counts was found to be insignificant except in cases of HIV retinopathy (p value=0.001), HIV microangiopathy (p value=0.020) and CMV retinitis (p value=0.01).

**Table 2: Correlation of ocular manifestations according to CD4 counts**

Ocular Manifestations	CD4 Count			Total (%)	P-Value
	1-100	101-200	>200		
Blephritis	2	6	15	23 (5.8)	0.647
Molluscum Contagiosum	1	1	10	12 (3)	0.511
Herpes Zoster Ophthalmicus	0	2	3	5 (1.3)	0.467
Corneal Opacity	0	0	5	5 (1.3)	0.401
Conjunctivitis	1	4	17	22 (5.5)	0.898
Dry Eye	8	5	14	27 (6.8)	-
External Hordeolum	0	0	2	2 (0.5)	0.872
Bell's Palsy	0	0	3	3 (0.8)	0.395
HIV Microangiopathy	5	7	13	25 (6.3)	0.020
Keratitis	0	2	7	9 (2.3)	0.555
Anterior Uveitis	1	1	4	6 (1.5)	0.667
Complicated cataract	2	2	2	6 (1.5)	0.59
CMV Retinitis	3	1	2	6 (1.5)	0.01
Toxoplasma Retinochoroiditis	1	2	4	7 (1.7)	0.8
Tubercular choroiditis	2	3	5	10 (2.5)	0.195
Non-Specific Choroiditis	3	6	15	24 (6)	0.375
HIV Retinopathy	9	7	21	37 (9.2)	0.001

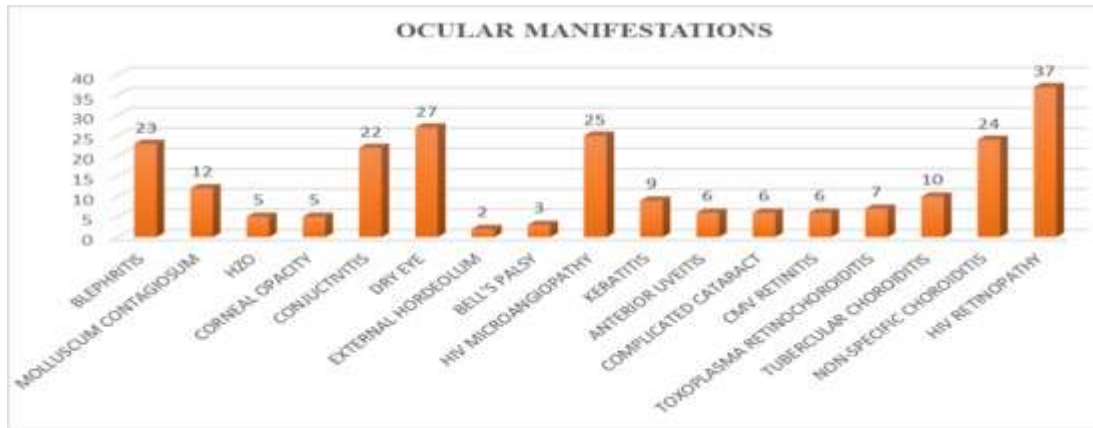


Fig. 4: Distribution of Ocular manifestations in HIV patients

Majority of the patients had mild visual (6/6-6/12) deterioration in this study i.e., 83.3% in right eye and 76% in left eye Moderate visual deterioration (6/18-6/36) in 11% of right eyes and 16.7% of left eyes of the total number of patients. Severe visual deterioration (6/60 or less) was seen in 5.7% in right eyes and 7.3% in left eyes of the 400 patients studied here. (Fig. 5)

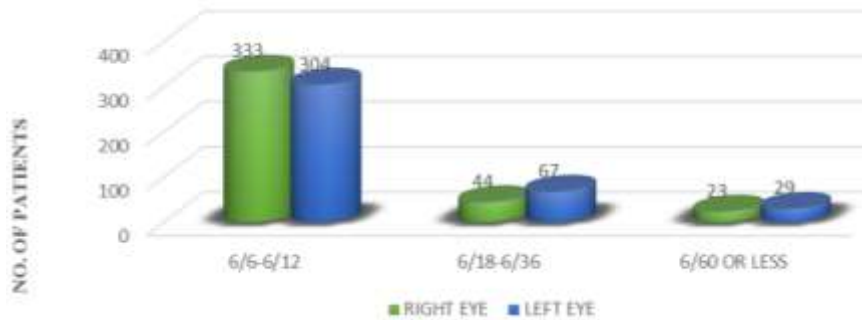


Fig. 5: Distribution of patients according to visual acuity in right and left side

**Discussion**

In the present study, out of 400 patients with HIV, 114 patients had ocular manifestations.

In present study, 28.5% patients had ocular manifestations, which is in concordance with the study by Nateshan CR et al (2011). Whereas the study done by Ganekal S et al (2012) et al. showed a higher prevalence of ocular involvement of 46% which may not be significant due to study done on a small group of patients, whereas the study by Astha singh et al (2012) showed 21.5% of prevalence whose results are nearer to our study. The reduced prevalence of ocular involvement in our study can be attributed to effective HAART Therapy. (Table 3)

**Table 3: Ocular manifestations in various studies**

Study	Prevalence (%)
Present study (2016)	28.5%
Nateshan CR et al (2011)	31.5%
Azonobi Richard Ifeanyi (2013)	14.0%
Sophia pathai et al (2009) <sup>(10)</sup>	17.5%
Ganekal S et al (2012)	46%
Shah et al (2009) <sup>(9)</sup>	8%
Astha singh et al (2012)	21.5%

The number of cases in the study by Sophia pathai et al (2009) is only 26 and hence the prevalence of ocular manifestations is different and high. The prevalence of ocular manifestations in relation to CD4 counts in the present study is not comparable to other studies shown here as maximum number of cases studied had CD4 count range of >200 cells/cu mm and the increased prevalence of ocular manifestations with decreased severity in terms of CD4 counts. (Table 4)

**Table 4: Patients studied in relation to CD4 count**

CD4 count range (cells/cu mm)	Present Study (N=400)	Douglas A Jabs et al <sup>(11)</sup> (2007) N=389	Sophia pathai et al (2009) N=26	Udaya kumar et al(2010) N=100
1-100	25(6.3%)	198(51%)	13(50%)	45(45%)
101-200	81(20.3%)	90(22%)	7 (26.9%)	28 (28%)
>200	294(73.5%)	101(26%)	6 (23.1%)	27 (27%)

Table 5 highlights the distribution of our patients according to the probable route of the transmission of the disease. Sexual route (95.5%) was the most common route involved, which is also seen in various other studies like Nateshan CR et al. (2011), Biswas J et al., Dinesh K Sahu et al. 18(4.5%) patients were victim to the disease due to perinatal transmission.

**Table 5: Distribution of cases by mode of transmission in various studies**

Study	Sexual Transmission	Perinatal Transmission	Other Modes
Present study	95.5%	4.5%	-
Nateshan CR et al (2011)	91.8%	5%	3.2%
Biswas J et al. (2000) <sup>(17)</sup>	70%	6%	-
Dinesh. K Sahu et al.(1999) <sup>(16)</sup>	73%	-	-

In our present study, HIV retinopathy being the most commonest ocular involvement 9.2%, which is also found to be the most commonest involvement in the studies conducted by the others .our study shows a similar prevalence of HIV retinopathy as of Gharai S,Venkatesh et al. (2008) The second most common manifestation being the Dry eye disorder. In our study, Dry eye disorder is seen in 6.8 % of the patients .The studies conducted in other parts of the world show a lower prevalence of Dry eye disorder in HIV patients. The prevalence of CMV retinitis was found to be 1.5%. The lesser prevalence of CMV retinitis compared to other studies may be attributed to the decline in the cases of CMV retinitis by the introduction of prompt and

aggressive HAART therapy. The prevalence of HZO in our study is around 1.3% which is similar to the study conducted by Nateshan CR et al. (2011) and BISWAS J et al. which was around 1.3% and 1% respectively, whereas studies by Udayakumar et al (2010) shows dissimilar results. The prevalence of Toxoplasma Retinochoroiditis is same as HZO i.e. 1.7% in our study which is almost the same as the other studies. Anterior Uveitis was seen in 1.5% of the patients in our study. Other studies showed prevalence of 2.5% Nateshan CR et al. (2011), 3% Biswas J et al. 2000 and 5% Dinesh K Sahu et al. Keratitis was seen in 9(2.3%) patients as that of Biswas J et al. (2000) study. (Table 6)

**Table 6: Ocular manifestations in various studies (%)**

Manifestations	Present study	Nateshan C. R. et al. (2011)	Biswas J. et al. <sup>(12)</sup> (2000)	Udaya Kumar et al (2010)	Gharai s, Venkatesh et al. (2008) <sup>(13)</sup>
HIV retinopathy	9.2	14.3	19	31	11
CMV retinitis	1.5	5	24	10	20
Toxoplasmosis	1.7	1.3	-	-	1
HZO	1.3	1.3	1	7	0
Anterior uveitis	1.5	2.5	3	8	5
Choroiditis	6	1.5	5	10	2
Dry eye	6.8	2.5	0	3	0
Molluscum Contagiosum	3	1	1	4	0
Keratitis	2.3	1	2	1	1

The maximum number of study patients had mild visual disturbance in the present study and also in various studies conducted worldwide. The severe visual disturbance is seen mostly in the patients with severe immunosuppression (less CD4 count).

**Table 7: Distribution of patients with respect to Visual Disturbance**

Vision	Present Study N=400		Udayakumar et al(2010) n=100		Juliet Otit-Sengeri et al (2010) <sup>(14)</sup> n=116	Lamichanne. et al (2009) <sup>(15)</sup> n=117	
	OD	OS	OD	OS	OD/OS	OD	OS
6/6-6/12	333 (83.3%)	304 (76%)	69 (69%)	75 (75%)	44 (38%)	107 (91.45%)	109 (93.16%)
6/18-6/36	44 (11%)	67 (16.7%)	15 (15%)	12 (12%)	29 (25%)	4 (3.41%)	4 (3.41%)
6/60 or less	23 (5.7%)	29 (7.3%)	16 (16%)	13 (13%)	43 (37%)	6 (5.12%)	4 (3.41%)

**Fig. 6****Fig. 7****Fig. 8**

## References

- UNAIDS UNAIDS report on the global AIDS epidemic.2013.
- Hogde WG, Seif SR, Margolis TP .Ocular opportunistic infection incidences among patients who are HIV positive compared to patients who are HIV negative. *Ophthalmology* 1998;105:895-900.
- India: HIV epidemiological situation and health sector response. National AIDS Control Organization, Ministry of Health, India.
- Holland GN, Pepose JS, Pettit TH, Gottlieb MS, Yee RD, et al. Acquired immune deficiency syndrome. Ocular manifestations. *Ophthalmology* 1983;90:859-873.
- Freeman WR, Lerner CW, Mines JA, Lash RS, Nadel AJ, et al. A prospective study of the ophthalmologic findings in the acquired immune deficiency syndrome. *Am J Ophthalmol* 1984;97:133-142
- Cunningham ET Jr, Margolis TP. Ocular manifestation of HIV infection. *N Engl J Med* 1998;339:236-44.
- Turner B J, Hect FM, Ismail RB. CD4+ T Lymphocyte measures in the treatment of individuals infected with Human Immunodeficiency Virus type 1: A review for clinical practitioners. *Arch Intern Med* 1994;154:1561-73.
- Biswas J, Raman R. Acquired Immunodeficiency Syndrome and Eye. Saxena S. *Clinical Practice in Ophthalmology*. 1st ed. New Delhi: Jaypee; 2003;286-305.
- Shah SU, Kerkar SP, Pazare AR. Evaluation of ocular manifestations and blindness in HIV/AIDS patients on HAART in a tertiary care hospital in western India. *British J Ophthalmol* 2009;93:88-90.
- Sophia Pathai, Alaka Deshpande, Clare Gilbert, Stephen D. Lawn. Prevalence of HIV-associated ophthalmic disease among patients enrolling for antiretroviral treatment in India: A cross-sectional study. *BMC infectious diseases* 2009;9:158.
- Douglas A. Jabs et al. Longitudinal study of ocular complications of AIDS. *Ophthalmology* 2007;114:780-786
- Biswas J, Raman R. Acquired Immunodeficiency Syndrome and Eye. Saxena S. *Clinical Practice in Ophthalmology*. 1st ed. New Delhi: Jaypee 2003;286-305.
- Gharai S et al. Ophthalmic manifestations of HIV infections in India in the era of HAART: analysis of 100 consecutive patients evaluated at a tertiary eye care center in India. *Ophthalmic Epidemiol*. 2008;15:264-71.
- Juliet Otit-Sengeri et al. The Prevalence and Causes of Visual Loss among HIV-Infected Individuals in Uganda. *J Acquir Immune Defic Syndr* 2010;53:95-101.
- Lamichhane G, Shah DN, Sharma S, Chaudary M. Ocular manifestations in HIV cases in Nepal. *Nepal J Oph* 2010;2: 45-50.

16. Sahu DK et al: Ocular manifestations of HIV infection/AIDS in South Indian patients. *Indian J Ophthalmol* 1999;47:79-85.
17. Biswas J, Raman R. Acquired Immunodeficiency Syndrome and Eye. Saxena S. *Clinical Practice in Ophthalmology*. 1st ed. New Delhi: Jaypee 2003;286-305.