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**Original article**

# Ophthalmic Manifestations of HIV Patients in Rural Setting – A Retrospective Study

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**Abstract**

**Introduction:** Among 40 million cases worldwide, 60-75% of patients have at least one ocular manifestation in their lifetime. The eye is an organ with wide spectrum of HIV-related manifestations. This study aimed to determine the pattern of ocular manifestations of HIV/AIDS and their correlation with CD4-count in a rural area of India.

**Materials and Methods:** A hospital based observational study was done on 212 HIV-positive patients presenting to ART center with ocular complaints. Data were collected using face-to-face interviews, clinical examination, slit lamp examination, fundus examination, and laboratory investigations.

**Results:** Out of 212 patients, 114 were males, and 98 were females, with mean age of 38.75 ± 13.9 years. HIV retinopathy was the most common HIV associated ophthalmic lesion, while anterior uveitis was the most common anterior segment finding. Posterior segment lesions showed a significant association with the low CD4 count of the patient. CMV retinitis, retinal detachment, tubercular chorioretinitis, and acute retinal necrosis were all seen in patients with CD4 count of less than 100 cells/mm3.

**Conclusions:** HIV retinopathy, CMV retinitis, herpes zoster ophthalmicus, and anterior uveitis are common ocular manifestations associated with HIV infection. Low CD4 count is a risk as well as a predictor for ocular manifestations. There needs to be awareness of ocular involvement among HIV infected individuals and an increased emphasis on regular ophthalmic examination.

**Keywords:** HIV, ocular involvement, CD4 count, HAART

## 1. INTRODUCTION

AIDS have been a major public health problem since the first case report in 1980.[1] It is a lethal multisystem disorder caused by a retrovirus, HIV.[1,2] The disease is having a diverse impact on human beings: affecting the economy, social life, education and people's health.[3] Patients with HIV/AIDS suffer from wide varieties of complications that are related to the infection. The eye is an organ with wide spectrum of HIV-related manifestations. The ocular manifestations can be the presenting sign of a systemic infection in an otherwise asymptomatic HIV positive person. The disease can have adnexal, anterior segment, posterior segment, orbital, and neuroophthalmic manifestations. The prevalence of HIV-related ocular manifestations increases as CD4+ T cells count decreases. Introduction of highly active anti-retroviral therapy (HAART) has changed the prevalence and pattern of HIV related ocular manifestation. HIV was first identified in 1986 in Chennai among commercial sex workers in India. At present the prevalence of HIV infected people in India is 2.5 million and worldwide it's about 65 million.

Ocular manifestations may be the initial presentation of a systemic infection in an asymptomatic HIV positive patient. Hence, early detection of the manifestations is critical, impacting the prognosis of the disease.[4,5] As part of our efforts to provide the



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best care to HIV patients, preventing visual morbidity in these patients because of ocular complications also needs to be addressed. Information regarding these ocular manifestations is unavailable from a rural areas of India. Till date, to the best of our knowledge, there has been no study indicating the ocular manifestations of HIV/AIDS from a rural areas of India. Hence, this study was undertaken to identify the ocular manifestations of HIV/AIDS in a rural area of western Maharashtra in India.

## 2. METHODS

***Study Design***. The present study was a hospital based observational cross-sectional study. It was carried out at the Department of Ophthalmology of Rural Medical College and Pravara Rural Hospital of Pravara Institute of Medical Sciences, Loni, from the period of August 2020 to August 2022. The hospital has an ART center affiliated to National AIDS Control Organisation (NACO) and catering to around 270 villages in the region.

***Inclusion Criteria***

1. Age ≥ 19 Years and < 70 years.
2. Newly diagnosed patients of HIV seropositivity, with blood investigation confirmed at Rural medical college loni.
3. Patients diagnosed as HIV positive outside centres who came to attend ART center are also included.
4. Patients referred from other departments to Rural medical hospital loni for screening purposes.

***Exclusion criteria***

1. Children and < 19 years.
2. Pregnant women
3. Persons who are terminally ill and unable to give consent due to Neuro behavioural problems.

***Data Collection***

Data was collected using interviews, clinical examinations, and laboratory investigations. Questionnaires were used for the interview and recording format were used for recording clinical examination findings. Eye examinations included; best corrected visual acuity test, intraocular pressure measurement, adnexal examination, pupil, motility, anterior segment, dilated fundus examination

The following tools were used for ophthalmic examinations; Snellen visual acuity charts, Jaeger near vision chart, Schiotz tonometer, indirect ophthalmoscope, slit lamp biomicroscope, 20D Volk lens, 90D Volk lens, and Goldmann three-mirror lens. Fundus fluorescein angiography, ultrasound examination, and other investigations such as magnetic resonance imaging were obtained in cases wherever necessary. For all patients who did not have CD4+ T cell count within three months before data collection, CD4 count was done during the study.

***Statistical Analysis***

Data were analyzed using SPSS version 13 software. Mean and standard deviation were used as descriptive statistical tools. Chi-square test ($\chi^2$-test) was used wherever possible to see association and $p<0.05$ was considered significant. A comparison of all the ocular manifestations were done in relation to the CD4 count in this presentation.

***Ethical Issues***

The study was conducted following the Helsinki declaration and after it was approved by the Institutional Ethical Committee and Research Cell of Pravara Institute of Medical Sciences. Written informed consent was taken from all the patients and only those who consented were studied.



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## 4. RESULTS

Table 1: Age distribution

| Age (in years) | No of cases |
|---|---|
| 19 – 20 | 3 |
| 21 – 30 | 27 |
| 31 – 40 | 70 |
| 41 – 50 | 75 |
| 51 – 60 | 27 |
| 61 – 70 | 10 |
| Total | 212 |
| Mean±S.D | 40.75±10.15 Years |

The age of the patients ranged between 19 years and 70 years with a mean age of 40.75 years ± 10.15 (standard deviation). Most of the cases were observed with 4th decade age. 35.38% cases were observed having age from 41 to 50 years of age, 33.02% cases had age from 31 to 40 years of age, 12.74% each case were observed in 2nd and 5th decade respectively,4.72% cases were seen having age from 61 to 70 years of age where only 1.42% cases had age less than 20 years of age. 40.75 years mean age was observed during the study period.

Table 2: Adnexal and Anterior segment manifestation /Association between ocular lesions and CD4-count

| Adnexal manifestation and Anterior segment lesions | Percentage of total patients (n=212) | CD4 Count (cells/m3) (Adnexal manifestation and Anterior segment lesions n-156) | | | | P Value |
|---|---|---|---|---|---|---|
| | | < 199 (n%) | 200 – 499 (n%) | > 500 (n%) | Total | |
| Blepharitis | 11.32 | 3 (1.92%) | 8 (5.12%) | 13(8.33%) | 24 | 0.34 |
| CV (Conjunctival microvasculopathy) | 9.43 | 14 (8.97%) | 6 (3.84%) | 0 | 20 | 0.04* |
| Molluscum contagiosum | 11.32 | 8 (5.12%) | 14(8.97%) | 2 (1.28%) | 24 | 0.46 |
| Dry eyes | 7.54 | 0 | 6 (3.84%) | 10(6.41%) | 16 | 0.24 |



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| | | | | | | |
|---|---|---|---|---|---|---|
| Giant papillary conjunctivitis | 6.60 | 0 | 4 (2.56%) | 10(6.41%) | 14 | 0.19 |
| Conjunctival SCC* | 3.77 | 6 (3.84%) | 2 (1.28%) | 0 | 8 | 0.32 |
| HZO Kaposi of lid | 0.94 | 1 (0.64%) | 1 (0.64%) | 0 | 2 | - |
| Kaposi of conjunctiva | 0 | 0 | 0 | 0 | 0 | - |
| Steven Johnson's syndrome | 0.94 | 0 | 1 (0.64%) | 1 (0.64%) | 2 | - |
| Anterior uveitis | **12.26** | 15 (9.61%) | 8 (5.12%) | 3 (1.92%) | 26 | 0.03* |
| Infectious Keratitis | 9.43 | 0 | 8(5.12%) | 12(7.69%) | 20 | 0.15 |
| Total | | 47 (30.12%) | **58 (37.17%)** | 51 (32.69%) | 156 | |

*SCC= squamous cell carcinoma. *HZO= herpes zoster ophthalmicus.

Table 3: Neuro-ophthalmic and posterior segment lesions/ Association between ocular lesions and CD4-count

| Posterior segment lesion | Percentage of total patients (n=212) | **CD4 Count (cells/m3) (Neuro-ophthalmic and posterior segment manifestations n-121)** | | | | **P Value** |
|---|---|---|---|---|---|---|
| | | < 199 (n%) | 200 – 499 (n%) | > 500 (n%) | Total | |
| Papilledema | 6.13 | 13(10.74%) | 0 | 0 | 13 | - |
| Facial nerve palsy | 0.94 | 0 | 1(0.82%) | 1(0.82%) | 2 | - |
| Optic neuritis or atrophy | 1.41 | 0 | 2(1.65%) | 1(0.82%) | 3 | 0.1 |
| 3rd Cranial nerve palsy | 1.41 | 0 | 3(2.47%) | 0 | 3 | - |
| CMV retinitis | **16.03** | 25(20.66%) | 9(7.43%) | 0 | 34 | <0.0001*** |
| HIV retinopathy | **14.15** | 26(21.48%) | 4(3.30%) | 0 | 30 | <0.0001*** |



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| | | | | | | |
|---|---|---|---|---|---|---|
| Toxoplasmosis retinochoroiditis | 5.66 | 0 | 12(9.91%) | 0 | 12 | - |
| Retinal detachment | 5.18 | 10(8.26%) | 1(0.82%) | 0 | 11 | - |
| Retinal vascular occlusions | 2.83 | 0 | 6(4.95%) | 0 | 6 | - |
| Retinopathy of anemia | 2.35 | 0 | 4(3.30%) | 1(0.82%) | 5 | - |
| Tubercular chorioretinitis | 0.47 | 1(0.82%) | 0 | 0 | 1 | - |
| Endogenous Endophthalmitis | 0.47 | 0 | 1(0.82%) | 0 | 1 | - |
| | | 75(61.98%) | 43(35.53%) | 3(2.47%) | 121 | |

Table 4: Segment of eye involved

| Visual acuity | Only adnexal and anterior segment | Only posterior segment | Only Neuro-ophthalmic lesions | Combination of adnexal/anterior posterior and neuro-ophthalmic lesions | Total |
|---|---|---|---|---|---|
| Better than or 6/12 | 90 (39.13%) | 15 (6.52%) | 7 (3.04%) | 15 (6.52%) | 127 (55.21%) |
| 6/18 to 6/60 | 25 (10.86%) | 23 (10%) | 10 (4.34%) | - | 58 (25.22%) |
| Worse than 6/60 s | 3 (1.30%) | 17 (13.07%) | 3 (1.30%) | 22 (9.56%) | 45 (19.57%) |
| Total | 118 (51.30%) | 55 (23.91%) | 20 (8.68%) | 37 (16.08%) | 230 |

A total of 130 patients (61.32%) had anterior segment lesions. 156 anterior segment and adnexal lesions were found among 130 patients (Table 2). The most common anterior segment finding was anterior uveitis (26 patients, 12.26%) (table 2) followed by molluscum contagiosum and blepharitis. A significant relation was observed between Conjunctival microvasculopathy and CD4 count, Anterior uveitis and CD4 count. Of 212 patients, 82 (38.67%) had posterior segment and neuro-ophthalmic lesions. A total of 121 posterior segment lesions were found among 82 patients (Table 3). CMV retinitis (16.3%) (table 3) was the most common opportunistic infection of the retina/choroid followed by HIV retinopathy. A significant relation was observed between CMV retinitis and CD4 count, HIV retinopathy and CD4 count. CMV was the most common posterior segment lesion observed. 16.03% cases were observed with CMV retinitis posterior segment lesion followed by 14.15% cases of HIV retinopathy, 6.13% cases with Papilledema, 5.66% cases of Toxoplasmosis retinochoroiditis, 5.18% cases of retinal detachment, 2.83% cases of retinal vascular occlusions, 1.41% each case of Optic neuritis or atrophy and 3rd cranial nerve

palsy, 0.94% cases of Facial nerve palsy and 0.47% each case with tubercular chorioretinitis and Endogenous Endophthalmitis posterior segment lesion. More than 75% of cases of CMV retinitis and HIV retinopathy were observed having CD4 count of less than 100 cells/$mm^3$ which shows statistically significant association between CD4 count and CMV retinitis, CD4 count and HIV Retinopathy. There was no significant association found between neuroophthalmic lesions and CD4 count. A total of 230 eyes had some ocular lesions at presentation. (Table 4) shows best corrected visual acuity in these eyes. The patient's eyes were divided into groups with visual acuity better than or 6/12, between 6/18 and 6/60, and worse than 6/60 depending on the severity of visual impairment in the eyes with ocular lesions.

## 5. DISCUSSION

AIDS is an infectious disease that affects people by causing opportunistic infections and neoplasia. It is caused by the continuous drop in CD4+ T cells. With a decline in CD4+ count, the immune system steadily deteriorates, and as the infection develops, symptoms including malaise, night sweats, fever, and cachexia begin to appear. For disease staging, the absolute CD4+ count assessment is essential. Despite the fact that HIV/AIDS is a multisystemic disease, HIV-positive individuals might experience eye issues at any moment. The prevalence of ocular manifestation in this study was found to be 25.3%.

The mean age in this current study was 40.75 years during the research period. The majority of the instances—75 cases—were seen to be between the ages of 41 and 50; 70 cases were between the ages of 31 and 40; 27 cases each were seen to be between the ages of 21 and 30; 51 to 60; 10 cases were between the ages of 61 and 70; and 3 cases were younger than or equal to 20.

Patients with HIV had a cumulative risk of 52-100 % getting at least one abnormal eye illness, according to Biswas et al.[1.] It was also claimed that 40–45% of HIV-positive people in India whom an ophthalmologist examines had at least one eye symptom. Cunningham and Margolis et al. [2] estimate that 70 to 80 % of HIV-positive individuals will eventually have an eye condition. Blepharitis, conjunctival microvasculopathy, molluscum contagiosum, dry eyes, giant papillary conjunctivitis, conjunctival SCC, HZO kaposi of lid, kaposi of conjunctiva, and Steven Johnson's syndrome were among the adnexal signs that were noted. Out of 212 cases in the current study, 11.32 % had blepharitis, of which 21.81 % had adnexal lesions; out of 9.43 % with CV, 18.88 % had adnexal lesions; and out of 11.32 % with Molluscum contagiosum, 21.88 % had adnexal lesions. 14.54 % with dry eyes out of the 7.54 % with dry eyes were found to have adnexal lesions. Adnexal lesions were present in 7.27 % of patients of conjunctival SCC and 1.81 % of cases with HZO Kaposi of the lid. Steven Johnson's syndrome cases with adnexal lesions were 1.81 % of all cases. Patients on HAART had a significant rate of ocular symptoms. This might be the outcome of patients being started on HAART when their CD4+ T cell count is less than 250 cells/l, which causes a low CD4+ T cell count. This study found that individuals may have experienced an ocular symptom before beginning HAART, and a low CD4 count is associated with a higher prevalence of this manifestation.

According to a study by Bekele et al. and colleagues,[3] blepharitis was the most common adnexal symptom of the eye (12.8%), followed by molluscum contagiosum (2.6%), conjunctival squamous cell carcinoma (2.3%), and conjunctival microvasculopathy (2.3%) (2.3 %). A total of 7.358 % had anterior uveitis anterior segment lesions, infections keratitis, and adnexal symptoms. Anterior uveitis was seen in 56.52 % of patients with anterior segment lesions, while infectious keratitis was seen in 43.47 %. In Neuro ophthalmic and posterior segment lesions cases 10.74% cases were observed with Papilledema, 1.65% cases with Facial nerve palsy, 2.47% each case with Optic neuritis or atrophy and 3rd cranial nerve palsy respectively, 28.09% cases of CMV retinitis, 24.79% cases of HIV retinopathy, 9.91% cases of Toxoplasmosis retinochoroiditis, 9.09% case of Retinal detachment, 4.95% cases of retinal vascular occlusions, 4.13% cases of Retinopathy anaemia, 0.82% each case of tubercular chorioretinitis and Endogenous endophthalmitis respectively. 39.13% cases were observed with only adnexal and anterior segment having visual acuity better than or 6/12, 6.52% cases of posterior segment were seen having visual acuity better than 6/12, 3.04% cases of Only neuroopthalmic lesions were seen with visual acuity better than or 6/12 and 6.52% cases of combination adnexal/anterior posterior and neuroopthalmic lesions



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were seen having visual acuity better than or 6/12. In cases with visual acuity from 6/18 to 6/60, 10.86% of cases were observed with Only adnexal and anterior segment, 10% of cases with only posterior segment, 4.34% cases with Only neuroopthalmic lesions. When visual acuity dropped below 6/60, 1.30 % had just adnexal and anterior segment lesions, 13.07 % had only posterior segment lesions, 1.30 % had only neuroopthalmic lesions, and 16.08 % had adnexal/anterior/posterior and neuroopthalmic lesions combined. The advanced stage of HIV infection, sometimes known as AIDS, is characterized by a sharp fall in CD4+ T-cell count (200 cells/L). One of the most common clinical features of HIV-positive patients is ocular symptoms, with various clinical phenotypes having a nearly complete impact on eye structure.

Ocular symptoms develop over the course of the HIV infection along with a significant reduction of CD4+ T cells.

In their recent study of ocular diseases in 1000 consecutive HIV-positive individuals in India, Sudharshan et al.[8] discovered anterior uveitis in 16% of the patients. Clinical analysis was used to identify the most likely reason for anterior uveitis. Since anterior uveitis is extremely uncommon as a result of CMV retinitis, the two cases of anterior uveitis that co-occurred with the disease were likely caused by immunological recovery rather than the CMV disease process itself. Following toxoplasma retinochoroiditis, one patient had "spill-over" anterior uveitis. Another patient experienced immunological recovery uveitis, characterised by a significant loss of vision and severe anterior uveitis and vitritis. Her CD4 count was 215 cells/mm3 when she started HAART 3 months ago, but it has since improved to 496 cells/mm3.

In the present study significant association was observed in cases of Blepharitis with relation to CD4 count (cells/mm$^3$) (p=0.009), in CV cases and CD4 count (cells/mm$^3$) association between 0.0004**, Molluscum contagiosum cases and their CD4 count (cells/mm$^3$) association between 0.0008*** and Giant papillary conjunctivitis and CD4 count (cells/mm$^3$) with P value of 0.05*.

CMV retinitis was the most prevalent ocular opportunistic infection seen in the study (12.5%). This frequency of CMV retinitis is comparable to that reported in other studies from India, such as those conducted by Gharai et al.[9] (20%), Pathai et al.[10] (11.9%), and Biswas et al. [1] (17 %).

However, research from Africa indicates that CMV retinitis occurs only extremely rarely (around 1% or less). In contrast to America and Europe, African countries have a lower prevalence of CMV retinitis. This may not necessarily be due to a lower incidence; rather, it may be because patients in these regions pass away from systemic opportunistic infections before their CD4-count drops too low to allow the development of CMV retinitis. In present study Significant association was observed between CD4 count and the CMV retinitis and HIV retinopathy cases.

## 6. CONCLUSION:

The most prevalent ocular manifestation of HIV is CMV retinitis, associated with low CD4 T-cell levels. Patients with an HIV serological diagnosis should be checked for ocular involvement and their CD4 level should be correlated for treatment and a better visual prognosis. There should be more awareness of ocular involvement among HIV-infected people, as well as a greater emphasis on frequent ophthalmic examinations.

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