

Original Research Article

Ocular manifestations in HIV/AIDS- Prevalence in South India

1.

ABSTRACT: Human immune deficiency virus (HIV) related ocular manifestations may affect 50-75% of HIV infected people worldwide at some point during the course of their illness.

Aim: To estimate the prevalence of Ocular manifestations in HIV patients attending the ART centre.

Place and Duration of the study: Anti Retroviral Therapy(ART) centre at Government general hospital and Department of Pharmacology, Siddhartha Medical College, Vijayawada, Andhra Pradesh in south India. The study was conducted for six months from January 2010 to June 2010.

Study design: This is a cross-sectional and observational study done on 1003 patients with or without ocular manifestations.

Methodology: All the patients were examined for anterior and posterior segment by using slit lamp and indirect ophthalmoscopy. Visual acuity was recorded in all patients.

Results: The prevalence of HIV associated ocular diseases was seen in 24.32 % of HIV patients. The most common findings were seen in anterior segment in 157(15.65%) patients followed by posterior segment in 87(8.67%) patients. 8.57% of conjunctival microvasculopathy, 1.59% of uveitis, 1.19% of herpes zoster and 0.89% of xerosis were the most common findings seen in the anterior segment. 2.47% of HIV retinopathy, 0.99% of chorioretinitis, 0.89% of cytomegaloviral retinitis, 0.69% of choroiditis, and 0.69% of optic atrophy were the most common posterior segment findings. Tuberculosis was the main systemic finding seen in 63 patients.

Conclusion: All these ocular findings are directly related to the severity of the clinical stage of the disease and to the severity of immunosuppression.

Key words: HIV, AIDS, Prevalence, anterior segment, posterior segment.

1. INTRODUCTION

Acquired immune deficiency syndrome (AIDS) is the most devastating disease complex that mankind has ever faced. It is caused by Human immuno deficiency virus (HIV) which belongs to the family Retroviridae and subfamily lentivirinae, shows great genetic diversity and breaks down human immune system leaving victim to vulnerable life threatening opportunistic infections, neurological disorders or unusual malignancies. [1] As per current US Centers for Disease Control and prevention (CDC) classification system for HIV infected adolescents and adults, AIDS patient is defined as 'any HIV infected individual with CD4+ T cell count of <200/ microlitre regardless of the presence of symptoms or opportunistic diseases'. [2] According to WHO (World Health Organisation) Clinical staging HIV/AIDS is classified into five groups as Primary HIV infection, Clinical stage I, II, III and IV.[3]

The number of people newly infected with HIV globally is continuing to decline, but national epidemics continue to expand in many parts of the world especially in developing countries. AIDS remains one of the world's most serious health challenges, even today in this era of HAART. A new era of hope has emerged in countries and communities across the world that had previously been devastated by AIDS. However, a world in which AIDS has been eliminated can only be achieved through renewed and sustained commitment and solidarity and only if the available evidence and limited resources are used as efficiently and effectively as possible. [4] Introduction of HAART has definitely prolonged the survival of AIDS patients but meticulous clinical examinations and better follow-ups can make the patients' quality of life better than before.

HIV affects all the systems of the body and produces various abnormalities. These manifestations are common in the course of HIV infection and may be the direct result of HIV, secondary infections, neoplasms or side effects of drug therapy, along with individual characteristics such as genetic predisposition, gender and age. [5] Among these, ocular manifestations are also common. HIV related ocular manifestations may affect 50-75% of HIV infected people worldwide at

some point during the course of their illness. This generally takes the form of opportunistic infections that can affect any of the ocular tissues from anterior segment to posterior segment.

There are a number of opportunistic infections associated with HIV infection. CMV retinitis is the most common ocular infection in AIDS and other intraocular infections that more frequently occur in patients with AIDS include syphilis, toxoplasmosis, tuberculosis, *Candida* infection, and cryptococcosis. These have to be differentiated from CMV infection. Herpesvirus infections other than CMV infection can also cause a viral retinitis in patients with HIV infection. Herpes zoster ophthalmicus may be an early sign of HIV infection. Herpes zoster retinitis accompanied by acute retinal necrosis and herpes simplex retinitis has occasionally been seen in patients with AIDS. These viral retinal infections are often difficult to differentiate clinically from CMV retinitis. However, these studies were completed early in the history of the AIDS i.e. pre HAART era (Highly Active Anti Retroviral Therapy) and the percentages may have been decreased after the introduction of HAART. Very few studies were reported after HAART era on the prevalence of various types of ocular manifestations and morbidity in HIV patients especially in developing countries like India, where there is paucity in reporting is observed. This indicates that the epidemiology of ocular manifestations in HIV infection is not well understood. These manifestations may be due to HIV infection or opportunistic infections or due to immune reconstitution after initiation of therapy or due to the ART(antiretroviral therapy) itself.

In this scenario, keeping the above facts in mind, a cross-sectional and observational study was conducted on 1003 HIV patients attending ART centre in Siddhartha Medical college/ Government General Hospital, Vijayawada, Andhra Pradesh, India to know the prevalence of various ocular manifestations in HIV patients.

2. MATERIALS AND METHODS

This was a cross sectional and observational study. The protocol was approved by the institutional ethics committee. Informed written consent was obtained from all the patients enrolled in this study in local language and for the patients less than 14 years the consent was obtained from the parents or guardians. This study was carried out at highly populated ART Centre, Siddhartha Medical College / Govt. General Hospital, Vijayawada functioning under NACO guidelines. The study was conducted for six months from January 2010 to June 2010.

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2.1. Inclusion criteria

2.1.1. Patients diagnosed with HIV/AIDS attending ART centre.

2.1.2. Patients of all ages were recruited.

2.2. Exclusion criteria

2.2.1. Patients with ELISA negative (HIV- negative) were excluded from the study.

2.3. Materials

2.3.2. A formulated questionnaire.

2.3.3. Torches

2.3.4. Snellen chart- literate and illiterate

2.3.5. Slit lamp

2.3.6. Direct and indirect ophthalmoscope

2.3.7. Loupes +20, +90 Ds

2.3.8. Mydriatics: tropicamide, cyclopentolate.

2.3.9. Scheme and sheet for fundus drawing

2.4. Methodology/Procedure

On average, about 50 patients were seen daily. Only 10 patients were selected for the study following the inclusion and exclusion criteria. The procedure was explained and those who gave consent were recruited in the study and the following examinations were done:

2.4.1. Visual acuity test with Snellen chart

- 79 **2.4.2.** Color vision test with Ishihara charts
 80 **2.4.3.** Anterior segment examination by Slit lamp
 81 **2.4.4.** Dilated fundus examination with mydriatics: 90 D slit lamp biomicroscopy and 20 D binocular
 82 indirect fundoscopy
 83 **2.4.5.** Medical records of patients were observed to obtain information on systemic diseases, HIV
 84 status, CD4 counts and anti retroviral therapy.
 85

86 **2.5. Statistics**

87 The data was recorded on a well structured questionnaire. Care was taken to minimize
 88 the risk for missing and erroneous data. Data was then cleaned and entered on a specially designed
 89 SPSS data analysis sheet. Data was analysed using Chi- square test and p value of less than 0.05
 90 was considered statistically significant.

91 **2.6. Limitations**

- 92 **2.6.1.** Laboratory tests like CD4 counts, renal function tests and histology for conjunctival tumours had
 93 already been done where appropriate. So, it was difficult to confirm some diagnosis or get the
 94 new tests done if needed. Some patients' diagnosis was made based on clinical judgement.
 95 **2.6.2.** Unable to estimate Viral RNA.

96 97 **3. RESULTS**

98 A total of 1003 patients were examined in the present study who attended a highly populated
 99 ART centre located in Vijayawada, Andhra Pradesh, South India which is functioning under NACO
 100 (National AIDS Control Organisation, India). Age distribution is shown in table no. 1. More number of
 101 patients (n=402) were in between 26 and 35 years of age group and next highest number of patients
 102 (n=379) were in between 36 and 45 years of age group. Chi-square value is 1.97, df (degrees of
 103 freedom) is 6 and $P = .922$.
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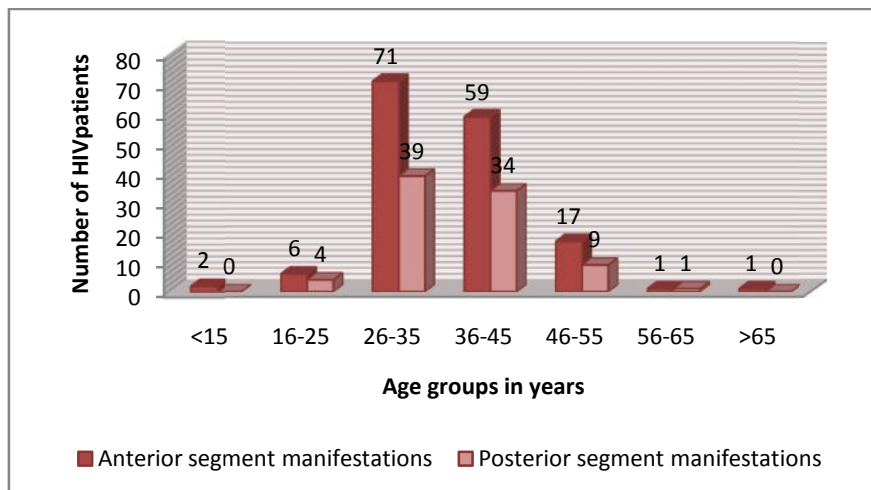


Fig no.1: Prevalence of Ocular manifestations in different age groups

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111 Male patients were 511 (50.9%) and female patients were 492 (49.1%). In male patients there
 112 were 85 anterior segment manifestations and 56 posterior segment manifestations, where as in
 113 female patients it was 56 and 31 respectively. Prevalence of HIV related ocular conditions were more
 114 in males. Chi-square value is 2.40, df is 1 and $P = .121$, which is not significant.

115 The number of patients in clinical stage III was 745, stage IV was 122 and stage V was 1.
 116 More patients were in stage III. The data is represented in fig no. 2. Chi-square value is 17.2, df is 4
 117 and $P = .002$ and is highly significant. Prevalence of ocular manifestations was more in Clinical stage III
 118 and also implies that ocular manifestations were more with progressing clinical stage of HIV disease.

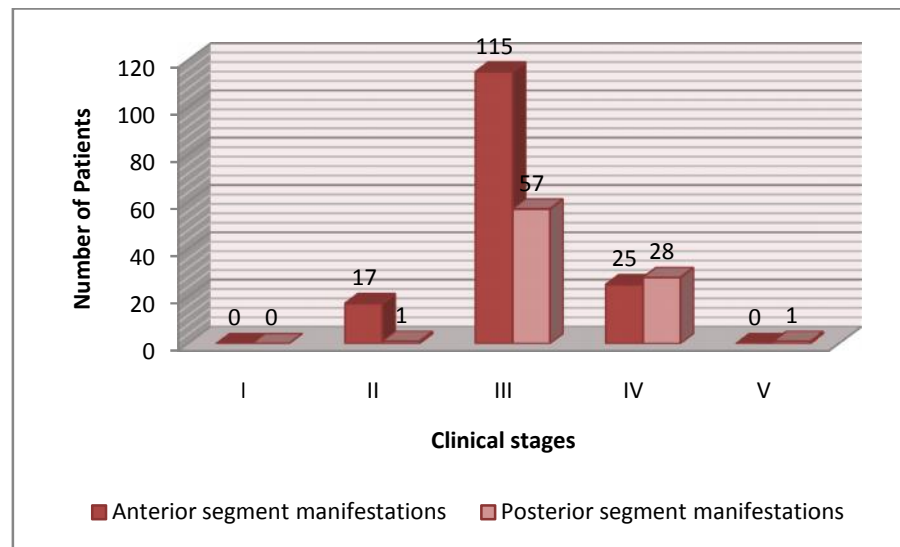


Fig no.2: Prevalence of ocular manifestations in different clinical stages of AIDS

The prevalence of HIV associated ocular diseases was 24.32%(244/1003). The most common findings were observed in the anterior segment in 15.65% of patients and 8.67% in posterior segment.

Various ocular manifestations in posterior segment and anterior segment were observed on ophthalmic examination. All the anterior segment manifestations and posterior segment manifestations are listed in table no.1 and table no. 2 respectively.

Table no.1: Various anterior segment manifestations and no. of patients affected.

S. No.	Anterior segment manifestations (ASM)	n=157(15.65%)
1.	Complicated cataract	11(1.09%)
2.	Conjunctival congestion	83(8.27%)
3.	Uveitis	16(1.59%)
4.	Episcleritis	4(0.39%)
5.	Herpes Zoster	12(1.19%)
6.	Xerosis	9(0.89%)
7.	Pthisis bulbi	5(0.49%)
8.	Chronic dacrocystitis	1(0.97%)
9.	Corneal opacity	4(0.39%)
10.	Hemiparesis	1(0.097%)
11.	Chicken pox	1(0.097%)
12.	Facial palsy	5(0.49%)
13.	Molluscum contagiosum	2(0.19%)
14.	Adherent leucoma	1(0.097%)
15.	Corneal ulcer	2(0.19%)

Table no.2: Various posterior segment manifestations and no. of patients affected

S. No.	Posterior segment manifestations (PSM)	n=87(8.67%)
1.	Chorioretinitis	10(0.99%)
2.	Vitreous opacities	4(0.39%)
4.	Acute retinal necrosis	5(0.49%)
5.	Optic atrophy	7(0.69%)
6.	HIV Retinopathy	25(2.49%)
7.	Choroiditis	7(0.69%)
8.	Cyto Megalo Viral Retinitis(CMVR)	9(0.89%)
9.	Tractional Retinal detachment	5(0.49%)
10.	Peripheral vasculitis	5(0.49%)
12.	Papillitis	1(0.097%)

14.	Retinitis	1(0.097%)
15.	Vitreous haemorrhages	2(0.19%)
16.	Macular oedema	3(0.29%)
17.	Papilloedema	3(0.29%)

More number of ocular manifestations [ASM= (n) 95 and PSM= (n) 48] were seen in patients with CD4 counts < 100 cells/mm³. As the CD4 counts decrease the prevalence of ocular manifestations was more as per the data shown in table no.3. Chi-square value is 7.42, df is 4 and $P=0.115$ (not significant).

Table no. 3: Number of ocular manifestations in HIV patients with different CD4 counts

CD4 COUNT In cells/mm ³	n	Anterior Segment Manifestations	Posterior Segment Manifestations	Total Ocular Manifestations n(%)
<100	332	59	48	107(10.6)
101 - 150	231	40	17	57((5.68)
151 - 200	191	26	11	37(3.68)
201 – 250	155	18	7	25(2.49)
>250	94	14	4	18(1.79)
Total	1003	157	87	244(24.3)

The HIV infected patients recruited in this study (n=830) were given different anti retro viral therapy regimens as ZLN (zidovudine+lamivudine+nevirapine), SLN (stavudine+ lamivudine+ nevirapine), ZLE (zidovudine+ lamivudine+ efavirenz) and SLE (stavudine+ lamivudine+ efavirenz) as per the NACO (National AIDS Control Organisation, India) guidelines. The rest of the patients (n=173) were not on any regimens as they were newly diagnosed cases and about to start the treatment. In these patients also ocular manifestations (PSM=13 and ASM=27) were noticed. Ocular manifestations were more in patients on ZLN treatment as shown in table no. 4. Chi-square value is 4.47, df is 4 and $P=.346$.

Table no. 4: Number of ocular manifestations in HIV patients taking different ART (Anti retroviral treatment) regimens

S. No	ART regimen	n	Anterior Segment Manifestations	Posterior Segment Manifestations	Total Ocular Manifestations n(%)
1.	ZLN	446	60	38	98(9.77)
2.	SLN	261	48	18	66(6.58)
3.	SLE	58	18	10	28(2.79)
4.	ZLE	65	14	6	20(1.99)
5.	ART not started	173	17	15	32(3.19)
6.	Total	1003	157	87	244(24.3)

Tuberculosis was the systemic manifestation seen in 156 HIV patients and they were on ATT (Anti tuberculosis treatment) as per RNTCP (Revised national tuberculosis control programme) guidelines. Ocular manifestations data is shown in table no.5. Chi-square value is 14.7, df is 1 and $P=.001$ which is significant.

Table no. 5: No. of patients with ATT and with ocular manifestations

S. No	Anti Tuberculous Treatment(ATT)	n	Anterior Segment Manifestations	Posterior Segment Manifestations	Total Ocular Manifestations n(%)
1.	Patients taking ATT	156	28	35	63(6.28)
2.	Patients without TB	847	129	52	181(18.04)
3.	Total	1003	157	87	244(24.3)

Visual acuity was tested for all the patients and complete blindness(bilateral) was seen in seven patients affected with CMVR(n=1), HIV retinopathy(n=1), Uveitis(n=1), Optic atrophy(n=1), acute retinal necrosis(n=1), Papilloedema(n=1), and Perivasculitis(n=1).

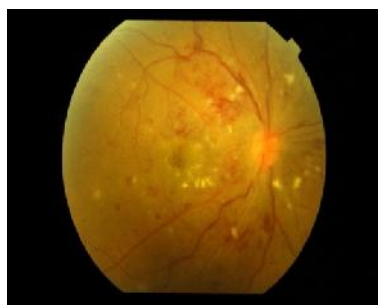


Fig no. 3: HIV retinopathy



Fig no. 4: CMV retinitis

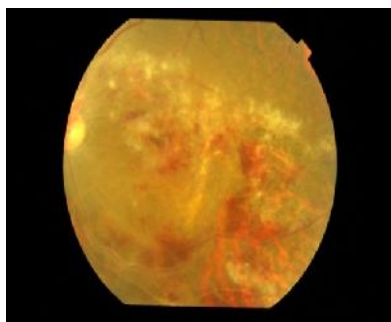


Fig no. 5: CMV retinitis

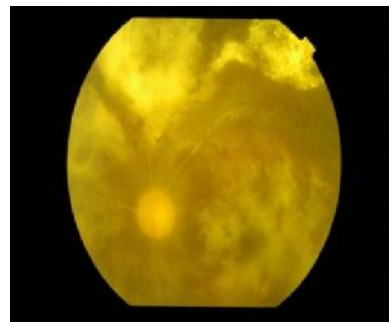


Fig no.6: Vasculitis and optic atrophy

4. DISCUSSION

HIV-1 infection, the cause of AIDS, is a worldwide pandemic with enormous adverse health and economic implications, particularly in the developing world. This bloodborne and sexually transmitted disease, which evolved from simian immunodeficiency virus, infects and replicates in helper T cells and macrophages and utilizes CD4 and a chemokine coreceptor for entry. Immune deficiency occurs as a result of virally induced attrition of CD4 T cells, resulting in the development of opportunistic infections and malignancy.[6]

Numerous ophthalmic manifestations of HIV infection may involve the anterior or posterior segment of the eye. Since the first report of the ocular manifestations of AIDS by Holland et al. in 1982, [7] subsequent studies have described several AIDS related conditions in the eye and orbit. More than 70% of adult AIDS patients will experience an ocular complication at some point of their illness. [8]

A study performed by Lamichhane et al. showed that ocular involvement was seen in 55 (47%) HIV/AIDS patients. [9] In this study the prevalence of ocular manifestations is 24.3%. This is comparable with the studies done by Gharai S et al, where in their study 45% (45/100) patients had ophthalmic manifestations, the most common being cytomegalovirus (CMV) retinitis (20%) (20/100). [10] But in this study, CMV retinitis was 0.89%(9/1003), this was comparable with the study done by

Elizabeth A et al, in which the CMV retinitis was 0.36/100 person years and the incidence was more with less CD4+ counts.[11]

As per Vraber TR et al, fifty-seven patients (28.5%) had ocular manifestations, and they showed significantly lower CD4+ T cell count than patients without ocular manifestations. [12] This is comparable with this study, as the incidence of ocular manifestations was 24.3% and more ocular manifestations were noticed with decreasing CD4+ counts. But there was no significant linear trend in the HIV positives with decreasing CD4+ counts as per the study of Dily Morgan et al. [13]

About 50% (19/40) patients had CD4+ count below 100 cells/micro liter and 70% (28/40) patients had CD4+ count below 200 cells/micro liter as per the study done byGharai et al., and this is comparable with this study where 40% patients had CD4+ counts<100 cells/micro litre and 38.6% with <200 cells/micro litre.

In general, the CD4⁺ T-lymphocyte count has been used to predict the onset of certain ocular infections in patients who are HIV positive. A CD4⁺ T-cell count below 500/mL is associated with Kaposi sarcoma, lymphoma, and tuberculosis. A CD4⁺ T-cell count below 250/mL is associated with Pneumocystosis and toxoplasmosis. A CD4⁺ T-cell count less than 100/mL is associated with Retinal or Conjunctival microvasculopathy, Cytomegalovirus (CMV) retinitis and Varicella-zoster virus (VZV) retinitis. [3]

The predictive value of the CD4⁺ T-cell count for ocular complications in HIV infection has been called into question by reports of HIV related ocular complications in patients with CD4⁺ cell counts more than 200 cells/mL. The patients reportedly were taking highly active antiretroviral therapy (HAART). While such findings are against the protective effect of an increased CD4⁺ cell count, the possibility that these manifestations preceded the recovery of CD4⁺ cell count. As seen in this study, there was significance regarding the prevalence of more ocular manifestations as the clinical staging of HIV progresses, when compared to the data seen with CD4 cell count. Thus, whether a reconstituted T-cell count will serve as a better predictor of specific ocular infection is under active evaluation.

The ocular findings seen in this study related to HIV infection are very less to draw any conclusions. CMV retinitis in this study was seen in 9(0.89%) patients, which is very less when compared with most of the previous studies where the incidence was from 20-40%.[11,12,14,15,16]

AIDS patients with Tuberculosis tended to have more retinal microangiopathy, but this was not statistically significant in the study done by Beare NAV et al., in African areas [17] where as in this study, the prevalence of ocular manifestations in patients with Tuberculosis and HIV was highly significant. These differences most likely result from different socioeconomic conditions and basic health care availability and from different patterns of endemic disease prevalent before the HIV/AIDS epidemic.

Due to the potentially devastating and rapid course of ocular infections, all persons with HIV disease should undergo routine ophthalmologic examinations. Any HIV-infected person who experiences ocular symptoms also should receive prompt and competent ophthalmologic care. Nonetheless, eye infections associated with sexually transmitted diseases (STDs) such as herpes simplex virus, gonorrhea and chlamydia are more frequent in HIV-infected patients. Therefore, clinicians should screen for HIV in the presence of these infections.

Fortunately, many of these infections are now treatable with therapeutic agents. Early recognition of these infections is important so that appropriate therapy can be instituted. Immune system recovery following initiation of antiretroviral therapy (ART) may modify clinical presentation of ocular infections and can affect response to treatment.

Therefore, HIV-infected patients still require close ocular follow up even if they are on HAART. Occasionally, HAART may cause vision loss via the mechanism of immune recovery uveitis. It may be characterized by vitritis and optic disc and macular edema.

5. SUMMARY AND CONCLUSION

Practising ophthalmologists, those in the developing world, where there is HIV pandemic, are faced with the following challenges. One, they must be able to diagnose and treat vision-threatening

conditions. Two, they must be able to identify unusual presentations. Three, ophthalmologists must be able to identify and document manifestations as early as possible in a HIV positive patients in the course of their disease and also during the treatment period.

The ART centres run by NACO, are not provided with adequate ophthalmic examinations. Thus, it is advisory to get all the HIV patients attending these centres to be examined for vision threatening complications, both medical and surgical ocular complications.

The study has to be done in more centres and more number of patients has to be included to confirm these findings.

COMPETING INTERESTS

All Authors declare that no competing interests exist.

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