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Original Research Article

A study of ocular manifestations in HIV positive patients

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ABSTRACT

Introduction: The present study aimed to determine the prevalence and pattern of ocular manifestation in HIV positive patients and to correlate ocular lesions with CD4 counts in HIV positive patients.**Materials and Methods:** The study was conducted as an observational study on seropositive HIV patients attending ART center and OPD department of ophthalmology during the study period of 2 years. Detailed sociodemographic and clinical history was obtained. Patients were subjected to thorough ophthalmologic evaluation and necessary investigations and findings were noted.**Results:** Ocular manifestations could be observed in 36 (52.2%) cases. Among them, unilateral ocular manifestations were observed in 11 (15.9%) cases and bilateral involvement in 25 (36.2%) out of 69 patients. A wide spectrum of ocular manifestations were observed, most commonly of posterior segment. Ocular manifestations were not significantly associated with CD4 count ($p > 0.05$) except CMV retinitis which was significantly associated with lower CD4 count (< 150 in 14.3% cases). Papilledema was significantly associated with higher CD4 count ($p < 0.05$).**Conclusion:** Ocular manifestations in HIV positive patients has a wide range of presentation. Every HIV patient must be educated about their ocular condition and should be advised to undergo regular ophthalmic examinations. Health care professionals also should be educated and trained in every aspect so as to pick up early cases of ophthalmic manifestations of HIV and should have coordination with ART center for easy assessment, detection and treating of vision-threatening ocular lesions at the earliest possible.This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.For reprints contact: reprint@ipinnovative.com

1. Introduction

Human Immunodeficiency Virus (HIV) was discovered in 1983 by Barre- Sinoussi Et Al.¹ According to the global statistics of 2020, released in June 2020, 38 million people are found to be HIV positive. In 2019 around 6.9 lakhs people have died from HIV related illness.² HIV prevalence in India in 2019 was estimated to be around 0.22% (23.49 lakhs). Mizoram has the highest prevalence with 2.32% and Tamil Nadu being 0.23%. In 2019 in estimated annual new HIV infections ranging between 2,000 to 3,000 in Madhya

Pradesh.

This infection gradually depletes CD4 lymphocytes, resulting in decreased blood levels of this crucial subset of “helper” T cells.³ Blindness due to HIV-related complications is a concern that endangering the life of people living with HIV. Its prevalence ranges from 6.9%-23%.⁴ The prevalence of HIV-related ocular manifestations are inversely proportional to CD4+ T cell count.⁵ By the introduction of highly active anti-retroviral therapy (HAART) it has changed both the prevalence and pattern of HIV- related ocular manifestation.⁶ Before HAART, CMV retinitis was the commonest ocular manifestation.⁷ In the HAART era, incidence of CMV retinitis, Kaposi’s

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sarcoma, retinal microvasculopathy and opportunistic retinal infections were also found to be lower.^{7,8} Ocular lesions usually occur in the late phase of the disease but can also occur in the early stages.⁹ These manifestations may be the initial presentation of a systemic infection in an asymptomatic positive patient.¹⁰ Early diagnosis and appropriate treatment can help in prevention of these sight threatening complications and thus decreasing the prevalence of blindness in these cases.

2. Objectives

1. To determine the prevalence of ocular manifestation in HIV positive patients attending ART center in Gandhi Medical College, Bhopal.
2. To evaluate the ocular manifestations of HIV positive patients.
3. Correlation of ocular lesions with CD4 counts in HIV positive patients.

3. Materials and Methods

The study was conducted as a hospital based Prospective Observational study at ART center in association with Department of Medicine and Department of Ophthalmology, Gandhi Medical College, Bhopal, Madhya Pradesh during the study period of 2 years i.e. from 1st November 2018 to 30th September 2020.

Seropositive HIV patients attending ART center; referred to department of ophthalmology for ocular complaints or attending ophthalmic OPD of Gandhi Medical College and willing to participate in the study were included whereas HIV patients with other congenital or pre-existing ocular diseases unrelated to HIV or history of trauma and not willing to participate in the study were excluded.

Before commencing the study, Ethics committee approval was obtained from the Ethics committee of Gandhi medical college, Bhopal. Informed and written consent was taken from all the patients. Socio-demographic data such as age, gender, socioeconomic status, occupation, marital status and place of residence was obtained from all the study participants and entered in questionnaire. For maintaining the confidentiality of the patient, UID number was allotted. Name of the patients were neither disclosed to any other person nor published in any written form. Even the registration number in the ART clinic which is unique to each patient was neither disclosed nor published. Instead the OPD number was used as the reference number. History of co-morbidities, mode of infection, duration of HIV infection, treatment history was obtained and entered in questionnaire. Patients were asked about the presence or absence of ocular symptoms.

The patient were subjected to thorough ophthalmologic evaluation which includes best corrected visual acuity determined using Snellen's chart; IOP determined using

Schiotz /applanation tonometer. A simple torch light examination performed to look at the lids and adnexa. Anterior segment examination was done on slit lamp which includes examination of Lid, Conjunctiva, Cornea, Anterior chamber, Iris, Pupil and Lens Anterior and Posterior segment examination was done on indirect ophthalmoscopy which includes examination of Vitreous, Choroid, Retina, Optic nerve. For dilatation one drop of phenylephrine and tropicamide was instilled at an interval of 10-15 minutes. After dilatation Fundus examination was performed with an indirect ophthalmoscope and 20 D or 28D lens.

Special investigations were done in certain cases such as Gonioscopy, Fluorescein Stain, Corneal Sensation and Schirmers Test, required for evaluation of anterior segment. Fundus photography, Fundus Fluorescein Angiography and Optical Coherence Tomography was done for evaluation of posterior segment.

The findings of investigations done in ART center were noted (CBC, ESR, CD4 COUNTS, LFT, RFT, USG ABDOMEN etc.). Additional investigation such as CMV serology and Histopathology of mass lesions were done in co-ordination with ART center whenever required.

All ocular findings were noted and the final ophthalmic status of patient were noted. In case of getting abnormal ophthalmic findings, it was examined and confirmed by senior ophthalmologist. Positive findings were treated according to standard management protocol.

Counselling was done regarding the ocular manifestations which may occur during the course of the disease and need for ophthalmic screening. The ophthalmic status was revealed to the patient after necessary counselling and need for periodic review was suggested.

3.1. Statistical analysis

Data was compiled using MS excel and analysed using IBM SPSS software version 20. Data was grouped and expressed as proportions. Chi square test was used to assess the association between proportions. P value <0.05 was considered statistically significant.

4. Results

In present study enrolled total of 69 patients of HIV fulfilling the inclusion criteria during the study periods.

The mean age of the study group was 36.8±12.05 years (Range-9 to 72 years). The proportion of Ocular manifestations were maximum in males (60.8%). Though, majority of patients with HIV were married (82.6%), proportion of ocular manifestations were maximum in widowed followed by unmarried patients. Majority of the patients with HIV belonged to lower socio-economic status (37.6%) and proportion of ocular manifestations were also higher in this socioeconomic group (66.6%).

Table 1: Distribution of patients and ocular manifestation according to demographic profile

| Demographic Characteristics | Frequency (n=69) | Percentage | No of patients with ocular manifestations | Proportion |
|-----------------------------|------------------|------------|---|------------|
| Age group (in years) | | | | |
| ≤20 | 4 | 5.8 | 2 | 50 |
| 21-40 | 43 | 63.7 | 17 | 39.53 |
| 41-60 | 20 | 27.5 | 15 | 75 |
| >60 | 2 | 2.9 | 2 | 100 |
| Gender | | | | |
| Male | 46 | 66.7 | 28 | 60.8 |
| Female | 23 | 33.3 | 8 | 34.78 |
| Marital status | | | | |
| Married | 57 | 82.6 | 28 | 48.28 |
| Unmarried | 10 | 14.5 | 6 | 60 |
| Widowed | 2 | 2.9 | 2 | 100 |
| Socioeconomic status | | | | |
| Lower | 26 | 37.6 | 18 | 66.6 |
| Lower middle | 17 | 24.6 | 8 | 47.05 |
| Upper lower | 7 | 10.14 | 3 | 42.8 |
| Upper middle | 16 | 23.18 | 6 | 37.5 |
| Upper | 3 | 4.3 | 1 | 33.33 |

Table 2: Distribution of according clinical history

| Variables | Frequency (n=69) | Percentage | No of patients with ocular manifestations | Proportion |
|--------------------------|------------------|------------|---|------------|
| Presentation | | | | |
| Symptomatic | 33 | 47.8 | 27 | 81.8 |
| Asymptomatic | 36 | 52.17 | 9 | 25 |
| Mode of infection | | | | |
| Heterosexual | 19 | 27.5 | 4 | 21.05 |
| Needle injury | 6 | 8.9 | 4 | 66.6 |
| Blood transfusion | 3 | 4.3 | 1 | 33.3 |
| Intravenous drug use | 5 | 7.2 | 3 | 60 |
| Perinatal | 2 | 2.8 | 1 | 50 |
| Unknown | 35 | 50.7 | 25 | 71.42 |
| Comorbidities | | | | |
| Tuberculosis | 12 | 17.4 | 8 | 66.6 |
| Tubercular meningitis | 3 | 4.3 | 3 | 100 |
| Herpes Zoster | 2 | 2.9 | 2 | 100 |
| Syphilis | 1 | 1.4 | 1 | 100 |
| RA and TB | 1 | 1.4 | 1 | 100 |
| Others | 6 | 8.6 | 4 | 66.6 |
| No comorbidities | 44 | 63.7 | 17 | 38.63 |

The proportion of ocular manifestations in asymptomatic patients is around 25%. However the proportion of ocular manifestation were more with symptomatic patients (81.8%). Higher proportion of ocular manifestations were noted in patients with unknown mode of transmission (71.42%). The proportion of ocular manifestations were more in patients who had associated tubercular meningitis, herpes zoster infection, syphilis and rheumatoid arthritis with tuberculosis (100%).

The proportion of ocular manifestations were more in those who had HIV infection with duration <1 year, non-compliant to HAART and with low CD4 counts.

Ocular manifestations were observed in total 36 (52.17%) patients. Among them, unilateral ocular manifestations were observed in 11 (15.9%) cases and bilateral involvement in 25 (36.2%) out of 69 patients. However 33(47.82%) patients had no ocular manifestations out of total.

Table 4 reveal ocular manifestations among patients with HIV. Ocular adnexal involvement was noted in 7(10.14%) patients whereas anterior segment and posterior segment manifestations were noted in 12(17.39%) and 21(30.43%) patients respectively. Neuro-ophthalmic manifestations was noted in 3(4.34%) patients.

Table 3: Distribution according to HIV characteristics

| Variables | Frequency (n=69) | Percentage | No of patients with Ocular manifestations | Proportion |
|--|------------------|------------|---|------------|
| Duration since diagnosis of HIV and initiation of HAART | | | | |
| <1 year | 7 | 10.1 | 6 | 85.7 |
| 1-5 year | 40 | 58.0 | 20 | 50 |
| >5 year | 22 | 31.9 | 10 | 45.45 |
| Compliance on HAART | | | | |
| Compliance | 63 | 91.3 | 32 | 50.79 |
| Noncompliance | 6 | 8.7 | 4 | 66.66 |
| CD4 count | | | | |
| 100-150 | 14 | 20.28 | 11 | 78.5 |
| 150-250 | 39 | 56.5 | 19 | 48.7 |
| 250-500 | 14 | 20.28 | 5 | 35.7 |
| >500 | 2 | 2.8 | 1 | 50 |

Table 4: Distribution according to ocular manifestations

| Ocular manifestations | Frequency (n=69) | Percentage |
|-------------------------------|--------------------------------------|------------|
| Ocular Adnexal manifestations | Herpes Zoster ophthalmicus | 2.8 |
| | Blepharitis | 1.4 |
| | Scleritis | 1.4 |
| | Conjunctivitis | 2.8 |
| | Conjunctival squamous cell carcinoma | 1.4 |
| | Total | 7 |
| Anterior segment | Dry eye | 2.8 |
| | Cataract | 5.7 |
| | Keratitis | 5.7 |
| | Anterior uveitis | 1.4 |
| | Glaucoma suspect | 1.4 |
| | Total | 12 |
| Posterior segment | Retinal microvasculopathy | 15.9 |
| | Posterior uveitis | 5.7 |
| | Age related macular degeneration | 2.8 |
| | Cytomegalovirus retinitis | 5.7 |
| | Retinal Detachment | 2.8 |
| | Total | 21 |
| Neuro-ophthalmic | Lateral Rectus paresis | 2.8 |
| | Papilledema | 5.7 |
| | Total | 3 |

Ocular manifestations were not significantly associated with CD4 count ($p>0.05$) except CMV retinitis which was significantly associated with lower CD4 count (<150 in 14.3% cases). Papilledema was significantly associated with higher CD4 count ($p<0.05$).

5. Discussion

Ocular manifestations in these patients were first documented by Maclean more than 20 years ago.¹¹ The ocular manifestations may result in opportunistic infections, vascular abnormalities, neoplasms, neuro-ophthalmic conditions, and adverse effects of

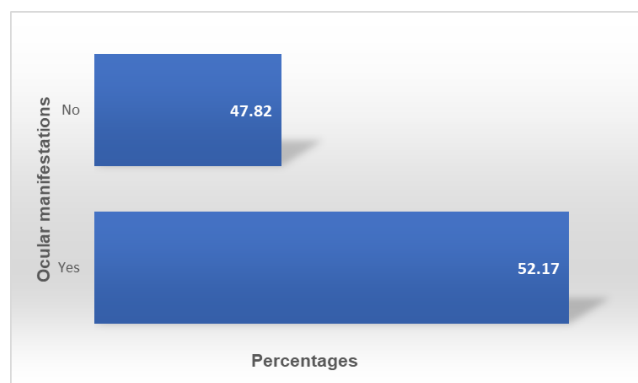
medications.¹¹

Our study observed prevalence of ocular manifestation in 52.2%, of them, bilateral involvement was noted in 36.2% cases. In study by Hothi et al¹² ocular symptoms were observed among 39% cases. In study by Ganekal et al¹³ 46% patients had ocular manifestations. Labh et al¹³ documented ocular manifestation in 40% patients.

Among adnexal manifestation, present study found Herpes zoster ophthalmicus, and conjunctivitis in 2.8% of the patients, whereas blepharitis, scleritis and conjunctival squamous cell carcinoma was noted in 1.4% patients. Rare case of scleritis in patients with HIV may be due to rheumatoid arthritis. In study by Sharma et al¹⁴ lid and

Table 5: Association of CD4 count with ocular manifestation in HIV patients

| Ocular manifestations | CD4 count | | | | χ^2 | P value |
|--------------------------------------|-----------|---------|---------|--------|----------|--------------|
| | 100-150 | 150-250 | 250-500 | >500 | | |
| Herpes Zoster ophthalmicus | 1(7.1) | 1(2.6) | 0(0) | 0 (0) | 1.389 | 0.708 |
| Blepharitis | 0(0) | 1(2.6) | 0(0) | 0 (0) | 0.781 | 0.854 |
| Scleritis | 1(7.1) | 0(0) | 0(0) | 0 (0) | 3.986 | 0.263 |
| Conjunctivitis | 0(0) | 1(2.6) | 1(7.1) | 0 (0) | 1.389 | 0.708 |
| Conjunctival squamous cell carcinoma | 1(7.1) | 0(0) | 0(0) | 0 (0) | 3.986 | 0.263 |
| Dry eye | 0 (0) | 2 (5.1) | 0(0) | 0 (0) | 1.584 | 0.663 |
| Cataract | 1 (7.1) | 3 (7.7) | 0 (0) | 0 (0) | 1.288 | 0.732 |
| Anterior uveitis | 1(7.1) | 0 | 0 (0) | 0 (0) | 3.986 | 0.263 |
| Keratitis | 2 (14.3) | 2(5.1) | 0 | 0 (0) | 2.864 | 0.413 |
| Glaucoma suspect | 0 (0) | 0 (0) | 1(7.1) | 0 | 3.986 | 0.263 |
| Retinal microvasculopathy | 2 (14.3) | 8(20.5) | 1 (7.1) | 0 (0) | 1.825 | 0.610 |
| Posterior uveitis | 0 (0) | 1(2.6) | 1 (7.1) | 0 (0) | 1.389 | 0.708 |
| ARMD | 0 (0) | 1(2.6) | 0 (0) | 0 (0) | 0.781 | 0.854 |
| CMV retinitis | 2 (14.3) | 0 | 0 (0) | 0 (0) | 8.092 | 0.044 |
| Retinal Detachment | 0 (0) | 2 (5.1) | 0 (0) | 0 (0) | 1.584 | 0.663 |
| Vasculitis | 1 (7.1) | 0 (0) | 0 (0) | 0 (0) | 3.986 | 0.263 |
| Vitritis | 0 (0) | 1 (2.6) | 0 (0) | 0 (0) | 0.781 | 0.854 |
| Endogenous Endophthalmitis | 1 (7.1) | 0 (0) | 0 (0) | 0 (0) | 3.986 | 0.263 |
| Lateral rectus paresis | 0 (0) | 1 (2.6) | 0 (0) | 0 (0) | 0.781 | 0.854 |
| Papilloedema | 0 (0) | 0 (0) | 1 (7.1) | 1 (50) | 18.14 | 0.001 |

**Fig. 1:** Prevalence of ocular manifestations in HIV patients

adnexal manifestations were seen in 8% patients, 3.3% patients had style and 1.3% of patients had molluscum contagiosum and HZO were seen in 1.3% in each. Blepharitis, Meibomitis, and entropion were seen in one patient each.

In study by Amsalu et al¹⁵ conjunctival squamous cell growth was seen in 3.8% of patients and blepharitis in 5% of patients. Thus it can be fairly said that Adnexal involvement is common in patients with HIV, most common form being lid involvement.

In the present study, anterior segment manifestations were noted in 17.39% patients, of them, Cataract was the most common (5.7%), keratitis and dry eye were noted in

2.8% cases each. of patients. Jabs et al¹⁶ also observed cataract as the leading cause of blindness in HAART era as incidence of Retinal detachment decreases due to HAART. Acharya et al¹⁷ documented lid infections as most common anterior segment manifestation followed by corneal opacity, Herpes zoster ophthalmicus, and Healed anterior uveitis.

The present study found Retinal microvasculopathy to be the most common posterior segment manifestation noted in 15.9% of patients whereas posterior uveitis and CMV retinitis was the next common ocular manifestation involving posterior segment observed in 5.7% of patients each followed by retinal detachment in 2.8% patients. The finding of present study were supported by findings of Pathai et al¹⁸ in which CMV retinitis was most common posterior segment manifestation in HIV patients which was significantly associated with low CD4 count. Similarly Acharya et al¹⁷ found HIV microangiopathy, followed by CMV retinitis as the most common manifestations in patients with HIV. Posterior segment involvement comes with angiopathies which is hardly reversed. As seen further, the involvement increases with loss of CD4 count, so measures need to be taken to maintain CD4 count so as to delay the posterior segment involvement and other complications.

Optic neuropathies in HIV patients may be due to inflammation, compression, infiltration, infection or vaso-occlusion lesions. Intracranial manifestations associated with HIV like Cryptococcal meningitis and intracerebral

toxoplasma cysts, can affect the eyes, and leads to nerve palsies. Neuro ophthalmic complications in HIV positive patient have also been reported in the absence of associated opportunistic infections.¹⁹ The present study found Neuro -ophthalmic manifestations in 3 (4.34%) patients. Acharya et al¹⁷ found hyperemic disc, pupillary abnormalities and papilledema as the common neuro ophthalmic manifestations in HIV patients.

Overall ocular manifestations were not significantly associated with CD4 count ($p>0.05$) except CMV retinitis which was significantly associated with lower CD4 count (<150 in 14.3% cases). Acharya et al¹⁷ concluded risk of Retinal microangiopathy, Conjunctival microvasculopathy, Keratoconjunctivitis sicca, VZV retinitis, CMV retinitis with progressive loss of CD4 count <100 cells/microlitre.

Singalavanija et al²⁰ found anterior segment involvement like dry eye, anterior and posterior blepharitis was higher in those with CD4 count 200- 500cells. CMV retinitis is manifested when the CD4 counts gets lower, between CD4 counts 200-500 cells mild ocular manifestations are seen as evidenced by above studies.

6. Conclusion

Ocular manifestations in HIV positive patients has a wide range of presentation and outcome from asymptomatic patients to permanent blindness. Blindness which can be prevented in a significant number of patients if properly managed and screened early. The posterior segment manifestations were found to be more prevalent. Every HIV patient must be educated about their ocular condition and should be advised to undergo regular ophthalmic examinations. Health care professionals also should be educated and trained in every aspect so as to pick up early cases of ophthalmic manifestations of HIV and should have coordination with ART center for easy assessment, detection and treating of vision-threatening ocular lesions at the earliest possible.

7. Strength of Study

1. As a result of screening, ocular manifestations were diagnosed at early stage and appropriate timely treatment was given which delay or reverse the ocularmorbidity.
2. Helpful in better understanding of presentation and clinical finding of ocular manifestations in HIV positivepatients.

8. Weakness of Study

1. Late presentation of patients at the studyarea
2. Maximum patients reported only when they have ocularmanifestations
3. Limited study period
4. Smaller samplesize

5. Covid-19 Pandemic affects the sample size taken for the study

9. Opportunities of Study

1. Repeated screening may lead to increase in awareness regarding ocular involvement in HIV patients

10. Source of Funding

None.

11. Conflict of Interest

The authors declare that there is no conflict of interest.

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