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Comparative study of ocular manifestations of HIV infection at a tertiary care hospital in Maharashtra, India

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Abstract

Purpose: *We conducted the study to observe the change in infection patterns with the introduction of highly active antiretroviral therapy (HAART) and correlation of CD4 count with various ocular manifestations of acquired immune deficiency syndrome (AIDS).*

Design*: This was a prospective observational cohort study.*

Methods*: The study was conducted at a tertiary care teaching institute with established antiretroviral therapy (ART) centre. A total of 240 eyes of 120 ART-naive patients were enrolled. Ocular manifestations of these patients were observed and followed up for six months for any change with HAART.*

Results: *Out of 240 eyes, 24 showed ocular involvement (10%), of which human immunodeficiency virus (HIV) microangiopathy and molluscum contagiosum were most common. Out of the four cases of HIV microangiopathy, two cases demonstrated complete resolution after six months of ART. Only one of three cases of cytomegalovirus (CMV) retinitis showed healing after six months of ART.*

Conclusions: *Vision-threatening CMV retinitis and herpes zoster ophthalmicus can improve if specific treatment is initiated promptly. There is direct correlation between CD4 count, ocular manifestation, and prognosis of the patients; 33.33% of patients showed improvement in ophthalmic manifestations after HAART during a follow-up period of 6 months.*

Keywords: *antiretroviral therapy, CD4 lymphocyte count, CMV retinitis, herpes zoster ophthalmicus, HIV infection, HIV microangiopathy*

Introduction

India is on the verge of being the country with the largest number of individuals living with human immunodeficiency virus (HIV)-acquired immune deficiency syndrome (AIDS). The total number of people living with HIV (PLHIV) in India was estimated at 2.117 million (1.711-2.649 million) in the year 2015.[1] Ocular lesions are also on the rise as the number of HIV-infected individuals is increasing.

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Ocular lesions were first reported in India in 1995 at Sankara Nethralaya, Chennai. The lifetime cumulative risk of developing at least one abnormal ocular lesion for a PLHIV ranges from 52% to 100% in various studies.[2] The epidemiological pattern of the disease in developed countries is different from that in developing countries. With the development of highly active antiretroviral therapy (HAART) in 1998, we witnessed a delay in illness and death, as well as a change in the pattern of ocular manifestations. The incidence of opportunistic ocular-infections causing retinitis has dramatically decreased, and clinicians should be aware of changes in the clinical manifestations of HIV. Pune and Mumbai are cosmopolitan cities with rising number of HIV-infected patients. At Pune, we run a well-equipped antiretroviral therapy (ART) plus centre, which has helped us in managing patients effectively.[4]

Materials and methods

The study was conducted at a tertiary eye care teaching institute from December 2008 to April 2011. Ethical approval was obtained from the ethics committee of our institute. Detailed evaluation of any ocular morbidity was conducted in 240 eyes of 120 HIV-naive patients who attended the ART centre of the institute after obtaining written consent from them. All patients underwent detailed history-taking which included World Health Organization clinical stage, CD4 count, and ocular symptoms at presentation.

A complete ophthalmological examination was performed including visual acuity examination, direct and indirect ophthalmoscopy and slit lamp microscopy, fundus fluorescein angiography, fundus photography, and B scan.

Inclusion criteria

1. Drug-naive patients diagnosed as having HIV infection by enzyme-linked immunosorbent assay test at the Integrated Counselling and Testing Centre.
2. Patients who are ART eligible as per National AIDS Control Organization criteria.

Exclusion criteria

1. Patients with pre-existing diabetic or hypertensive retinopathy.
2. Patients initiated on ART from private centres or patients who were exposed to ART drugs at any point of time.
3. Patients on ART who were lost to follow-up during the study.

Patients were followed up for six months on a monthly basis. CD4 count and ocular manifestations were compared using paired t-test and chi-square test.

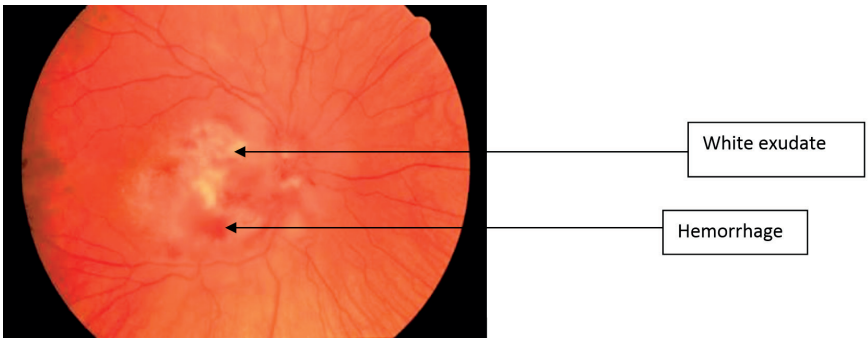
Observations and results

The age of the population included in the study ranged ffrom 2 to 70 years. Most patients fell (62.5%) within 21 to 40 years of age. Males predominated in the 120 patients, of which 24 had ocular involvement. The mean CD4 count pre-HAART was 140; post-HAART was 221.

We observed that low CD4 count patients (<100) presented more commonly with severe vision-threatening manifestations in the pre-HAART group (cytomegalovirus [CMV] retinitis, HIV retinopathy, herpes zoster ophthalmicus [HZO]). Some ocular manifestations are shown in Figures 1A, B and 2.

Molluscum contagiosum and HIV microangiopathy were the most common presentations. Patients who had received ART for more than two months showed a reduction in infection rates, although statistically insignificant.

A.



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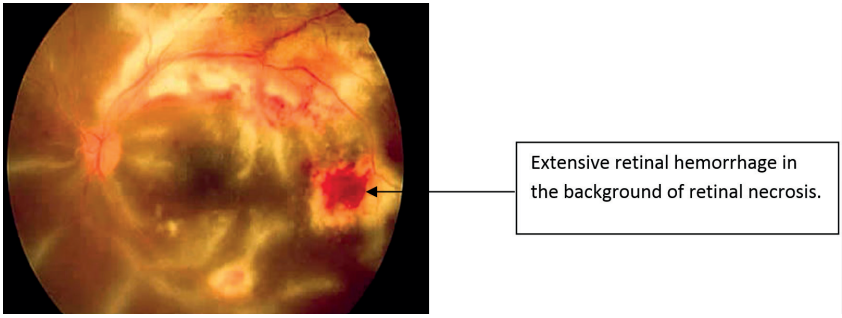

Fig. 1. Fundus photograph in case of CMV retinitis.

Table 1. Comparison of ocular manifestations in AIDS

Manifestation	Pre-ART (n = 120)	Follow-up (n = 105)
HIV microangiopathy	5 (4.17%)	3 (2.85%)
Molluscum contagiosum	4 (3.33%)	2 (1.90%)
CMV retinitis	3 (2.5%)	2 (1.90%)
Keratoconjunctivitis sicca	3 (2.5%)	2 (1.90%)
HZO	2 (1.67%)	1 (0.95%)
Orbital cellulitis	2 (1.67%)	0
Fungal ulcer	1 (0.83%)	1 (0.95%)
Blepharitis	1 (0.83%)	0
Conjunctivitis	1 (0.83%)	1 (0.95%)
Neuro-ophthalmic signs	1 (0.83%)	0
Choroiditis	1 (0.83%)	0
Vitritis	0	1 (0.95%)
Immune recovery uveitis	0	1 (0.95%)
Drug reaction	0	1 (0.95%)
Stevens-Johnson syndrome	0	1 (0.95%)
Any ophthalmic manifestation	24 (20%)	16 (15.23%)

Association between CD4 count and ocular manifestation at presentation

Tables 1 and 2 summarize our results. Molluscum contagiosum was observed in four cases and all had CD4 ranging between 100 and 250. HIV retinopathy and HZO were noted in patients with CD4 below 100. CMV retinitis was evident in cases with CD4 < 50. CD4 count improved after initiation of ART. In half the cases of HIV microangiopathy, fundoscopic changes were normalized.

Discussion

Our study described the ocular manifestations in patients with HIV-AIDS and the change in the pattern of the disease with HAART. When the gender distribution of study cases is taken into account, a male preponderance was noted. In their study in Western India, Shah *et al.* have also reported a greater number of male patients

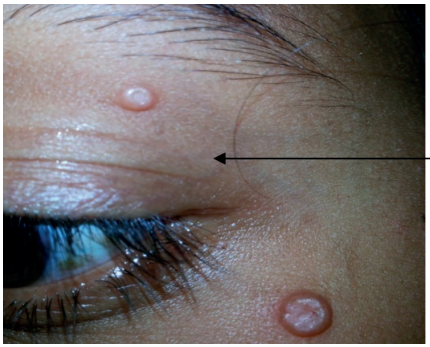

Fig. 2. Molluscum contagiosum.

Table 2. Pre- and post-ART manifestations.

Sl. No.	At the time of screening		On follow-up	
	CD4	Ophthalmic manifestation	CD4	Ophthalmic manifestation
1.	69	HIV microangiopathy	244	HIV microangiopathy
2.	22	HZO Dendritic ulcer	66	Keratitis
3.	34	CMV retinitis	56	Healed
4.	82	HIV microangiopathy	99	Normal
5.	60	HIV microangiopathy	123	Normal
6.	58	HIV microangiopathy	68	HIV microangiopathy
7.	141	Normal	313	Immune reconstitution uveitis
8.	64	Keratoconjunctivitis sicca	190	Keratoconjunctivitis sicca
9.	44	Keratoconjunctivitis sicca + CMV retinitis	Death	Keratoconjunctivitis sicca + CMV retinitis
10.	184	HIV microangiopathy	196	HIV microangiopathy
11.	115	Orbital cellulitis		Death
12.	130	Fungal ulcer	304	Healing fungal ulcer
13.	139	Keratoconjunctivitis sicca	296	Keratoconjunctivitis sicca
14.	76	HZO	–	Death
15.	33	CMV retinitis	40	CMV retinitis

with ocular infection. The difference between male and female number of cases could be due to increased prevalence of HIV infection in males. Secondly, females are deprived of screening modalities due to socioeconomic factors.

We recorded the maximum age of study patients to be 70 years and minimum age to be 2 years. The mean age was 33.4 years and median age was 35 years. Most cases (87.5%) fell in the group between 20 and 50 years of age. Of the total 120 cases, 73 (60.8%) were male and 47 (39.2%) were female.

Biswas *et al.* concluded that the cumulative risk of at least one abnormal ocular lesion developing in HIV-infected patients is 52-100%. It was also pointed out that 40-45% of HIV-infected patients in India have at least one ophthalmic manifestation when examined by the ophthalmologist. Cunningham and Margolis reported that 70-80% of HIV-infected patients had ophthalmic disease at some time during their lifetime. Table 3 compares the prevalence of ocular manifestations in our study with various other studies.

The prevalence of ocular manifestations is certainly on a declining trend owing to the rise in patients on ART and widespread availability of antiretroviral drugs through public health systems. Molluscum contagiosum and HIV microangiopathy were the most common ocular findings in the anterior segment, while CMV retinitis was the most common finding in the posterior segment. HIV microangiopathy showed significant response to HAART.

The mean CD4 count in the pre-HAART group was 140,whereas in the post-HAART group it was 224, which was statistically highly significant ($p < 0.001$ by paired t-test). It proves beyond doubt that HAART is playing a major role by increasing the CD4 count, and thus, life expectancy. All three cases of CMV retinitis were observed in patients with CD4 count < 50. Herpes zoster and HIV retinopathy occurred at CD4 count of less than 100. Only one case of immune reconstitution uveitis was noted in a patient from the post-ART group. It responded well to glucocorticoid therapy. In this patient, there was a rise in CD4 count from 141 to 313. Ocular lesions were observed in 24 patients in the pre-HAART group and 16 in the post-HAART group. In patients with ocular lesions, the median CD4 was 70 before initiation of HAART and 156.5 after initiation of HAART. This finding was highly significant statistically ($p = 0.006$ by paired t-test), emphasizing the pivotal role of HAART in reducing ocular morbidity and improving the quality of life.

Table 3. Prevalence of ocular manifestations in the present study with other studies

Manifestation	Holland *et al.*	Khadem *et al.*	Jabs *et al.*	Lim *et al.*	Kestelyn *et al.*	Our study
Sample size	30	08	200	118	20	120
Ocular involvement	63%	50%	25%	37%	55%	20%

In CMV infection, early retinitis was seen as small, white perivascular retinal infiltrates or dot-blot haemorrhages. The classic lesion is a hemorrhagic necrotizing retinitis that follows the retinal vasculature. Fluffy retinal infiltrates and necrosis are usually associated with scattered hemorrhages ("scrambled eggs and ketchup" appearance) (Fig. 1A and B).

Twenty-four of 120 patients in the pre-ART group had ocular manifestations, while 16 of 105 patients in the post-ART group had ocular manifestations. In the post-ART group, the ocular manifestations decreased and the types of manifestations were different, although not clinically significant. CMV retinitis and keratoconjunctivitis sicca, which have permanent sequelae, were counted in both groups, as this is a follow-up study.[12,13] Thus, prevention of ocular scar formation is of great relevance. ART initiation has been pivotal in the overall reduction of opportunistic infections.[14,15]

Conclusions

The prevalence of ocular manifestations decreased in the post-HAART group. Molluscum contagiosum and HIV microangiopathy in the anterior segment and CMV retinitis in the posterior segment were the most common presentations in the pre-HAART group, while Stevens-Johnson syndrome and immune recovery uveitis were specific to the post-HAART group. On comparing ocular manifestations in the pre- and post-HAART group, it was observed that the severity of ocular disease significantly declined in the post-HAART group. To conclude, availability of HAART treatment, screening from various specialties and experts through cross-reference after enrolment are necessary to prevent disastrous complications of the disease. As far as ocular manifestations are concerned, early diagnosis and follow-up will help the patient have a better visual prognosis and prevent vision-threatening complications.

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