Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/15293
DOI URL: http://dx.doi.org/10.21474/IJAR01/15293

RESEARCH ARTICLE

A STUDY OF OCULAR MANIFESTATIONS IN HIV/AIDS PATIENTS ATTENDING ART CENTRE AT TERTIARY CARE HOSPITAL OF SOUTH GUJARAT

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Manuscript Info

Manuscript History
Received: 27 June 2022
Final Accepted: 30 July 2022
Published: August 2022

Key words:-
HIV/AIDS, HAART, Ocular Manifestations, CMV Retinitis, Dry Eye, CD4 T Cell Count

Abstract

Introduction:AIDS is a multisystem disease, which can affect any part of the eye& can lead to significant morbidity and mortality. Around 40-70% of patients with HIV infection develops one of the ocular manifestations during lifetime. Introduction of HAART had significantly reduced occurrence of opportunistic infections and neoplasia in these patients.

Purpose: This study was conducted to study various ocular manifestations in HIV patients and to find out their prevalence and correlation with CD4 T Cell count.

Material & Methods: We conducted a Cross-Sectional Study on 100 confirmed HIV patients taking HAART. We conducted detailed ocular examination of these patients including vision assessment, IOP measurement, slit lamp examination and fundus examination. CD4 T Cell count and Duration of the Disease was also noted.

Results: We found 52% prevalence of HIV related ocular manifestations. Anterior Segment manifestations were more common than Posterior Segment. Dry Eye was the most common ocular finding accounting for 44.23% of the patients with ocular manifestations. Other Anterior Segment diseases included Cataract, Conjunctival Microvasculopathy, Blepharitis, Stye, Pterygium, Allergic Conjunctivitis, Anterior Uveitis and Viral Keratitis. Only 7 patients had Posterior Segment Diseases. 1 patient each of CMV Retinitis and PORN was seen, both having CD4 T Cell count below 100 cells/µl. Occurrence of these ocular manifestations were not related to age & gender of the patient or to the duration of the disease.

Conclusions: All patients with HIV should undergo Ophthalmic examination, irrespective of the CD4 T Cell count, Duration of Disease or presence of symptoms. Screening help in detecting these ocular diseases at early stage and thereby with early initiation of appropriate treatment help in reducing the visual morbidity.

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Introduction:-

Acquired Immunodeficiency Syndrome (AIDS) caused by Human Immunodeficiency Virus (HIV), a single stranded RNA virus that belongs to the subgroup Lentivirus of family Retroviridae. The virus infects T-Lymphocytes resulting in profound immunodeficiency leading to opportunistic infections and neoplasm.AIDS with its multisystem manifestations calls for an increasing attention in understanding the disease and managing it and the associated opportunistic infections.

The first case of HIV infection was detected in 1981 in world & in 1986 in India. Since then, this infection is rapidly spreading around the world from high-risk population to the general population. Globally in 2020, total HIV patients were 37.7 million. [1]

While in India around 23.48 lakh HIV patients were noted in 2019[2], third largest population of people living with acquired immunodeficiency syndrome in the world. [5]

In Gujarat, in the year 2019, 1.04 lakh people were living with HIV. [2]

Ocular involvement has been a common finding in these patients and loss of vision is a serious problem in people living with HIV. [19]

Around 40-70 % patients with HIV infection develops one of the ocular manifestations during lifetime. [3]

Ocular involvement in HIV was first described by Holland et al. in 1982, in the form of cotton wool spots, Cytomegalovirus Retinitis (CMVR) and Kaposi Sarcoma (KS).[13]

In India, the first case of AIDS with ocular lesions reported had CMV retinitis along with dementia in 1995. [5]

Ocular lesions usually occur in late stage of disease, but can also occur in early stage [5]& sometime it can be the presenting manifestation of systemic infection.[6] The spectrum of HIV associated ophthalmic disease ranges from adnexal disorders to anterior segment, posterior segment disorder to optic nerve and optic tract involvement.[7]

These manifestations can be a result of direct HIV infection or it can be opportunistic infection or drug related reaction [4]

Posterior segment involvement is more common & it is mainly responsible for visual morbidity.[7] CD 4 T cell count has been found to correlate with ocular lesions.[7] CMV retinitis remains the most common opportunistic infection in these patients [9]& usually seen with CD 4 T cell count <100 cells /µl. [7]The posterior segment complications usually lead to severe visual impairment or blindness if not detected and treated early.

With the advent of HAART in around 1995, there has been a significant improvement in the systemic and hence the ocular status of HIV infected individuals. [8]

In Pre-HAART era, ocular manifestations were estimated to affect around 50-75% of HIV patients [14] which has fallen to around 40% with HAART therapy, with almost 80% decline in incidence of CMV Retinitis.[8]

This has led to a paradigm shift from infectious to other non–infectious manifestations along with a noticeable change in the previously described classical phenotypic presentations of ocular opportunistic infections with HAART [4]

Introduction of HAART has led to dramatic decrease in HIV related morbidity and mortality with emerging condition of Immune related uveitis and drug toxicity.[10] Therefore, all patients with HIV must be thoroughly examined by ophthalmologist as early detection of these condition has major impact on prognosis. [11]

Materials and Method:-

It was a cross sectional study conducted at GMERS Medical College and Hospital, Valsad, Gujarat during the period of November 2020 to August 2021. The study was approved by Institutional Human Ethics Committee as well as Gujarat State AIDS Control Society.

The study included 100 HIV confirmed patients taking Highly Active Anti-Retroviral Therapy (HARRT) between the age group of 18-65 yrs who were willing to give written informed consent.

Patients with pre-existing illness like Diabetes, Hypertension, Age Related Macular Degeneration or severely ill/ comatose patients were not included in the study.Pregnant females and those patients on long term steroid/immunosuppressive treatment for other medical/surgical cause were also excluded from the study.

After obtaining written informed consent, each patient was subjected to detailed history taking including duration of HIV disease and Treatment, recent CD4 T Cell count, history of Tuberculosis and any active ocular complaints.

Patients were divided into 6 groups based on CD4 T Cell count (≤50, 51-100, 101-150, 151-200, 201-500,>500 cells/µl).

Ocular examination was performed on each patient irrespective of presence of ocular complaints, which included visual acuity and BCVA, IOP measurement by Non-ContactTonometry, Schirmer's test, corneal sensations. Slit lamp examination for Adnexa and Anterior Segment as well as Dilated Fundus examination with Indirect Ophthalmoscope.

Patients were advised appropriate treatment if any ocular disease found.

Patient's identity and examination findings were kept confidential.

All the data were recorded in a tabulated form in MS Excel sheet and relationship between various parameters were checked. Chi Square Test was applied to analyze the data using p value of <0.05 at 95% confidence interval.

Result:-

Out of the 100 HIV positive patients, 54 were Males and 46 were Females. The mean age of this study population was 43.71 yrs with highest number of patients (61%) in the age group of 36-55 yrs. Age and Gender distribution in the study was not statistically significant (p value >0.05).

The study included patients from recently diagnosed HIV to up to 20 yrs of disease and treatment.6 patients (54.5%) out of 11 recently diagnosed (<6 months) patients were having ocular manifestations.

Maximum patients (48%) had CD4 T Cell count in the range of 201-500 cells/µl. Average CD4 T Cell count of the study population was 506 cells/µl, with lowest value being 44 and highest being 1392 cells/µl. Only 8 patients were having CD4T cell count below 200cells/µl. CD4 T Cell counts among male and female patients were not significantly different (p value 0.542).

Raised Intra Ocular Pressure was observed in eyes with Anterior Uveitis and Mature cataract.

In this study we found that 52 patients were having ocular manifestations related to HIV disease, while 48 patients were having normal ocular examination findings.2 patients were having both Anterior and Posterior Segment Findings.

28 (53.84%) out of these 52 patients with HIV ocular manifestations were male and 24 were females (46.15%). Among 47 patients with Anterior Segment disease, 53.2% were male and 46.8% were females.In7 patients with Posterior Segment disease, 57.1% were male and 42.9% were female.Occurrence of ocular manifestations of HIV was Not Significantly different among male and female patients. (p value 0.97).

63.46% of the ocular manifestation was seen in the age group of 36-55 years (33 patients).

In 52 patients with ocular manifestations, 23 patients (44.23%) had Dry Eye, based on Schirmer 1 Test, which was the most common ocular manifestation related to AIDS observed in our study. 10 patients each of Mild and Moderate Dry eye with average duration of disease of 7.2 and 7.95 yrs respectively & 3 patients had Severe Dry Eye, all were females, with 10.33 yrs of average disease duration. Average duration of disease was found to be more for severe dry eye group, but it was NOT found to be statistically significant (p value 1.0)

Table 1:- Ocular Manifestations observed in Our Study: (N=52).

	No of Patients	Percentage
Anterior segment & Adnexal manifestations:		
Blepharitis	3	5.76
Stye	2	3.84
Pterygium	3	5.76
Allergic conjunctivitis	1	1.92
Conjunctival microvasculopathy	2	3.84
Viral keratitis	1	1.92
Anterior Uveitis	2	3.84
Glaucoma (angle closure)	1	1.92
cataract	15	28.84
Dry eye	23	44.23
Pupil sparing 3rd nerve palsy	1	1.92
Ciliary & Intercalary Staphyloma + leucomatous corneal opacity	1	1.92
Posterior Segment manifestations:		
CMV Retinitis	1	1.92
PORN	1	1.92
Old Retinal Detachment (Post CMV Retinitis)	1	1.92
HIV Retinopathy	2	3.84
Macular Scar	1	1.92
IT-BRVO with Macular Oedema	1	1.92

22 eyes of 15 patients were having significant cataractous changes (Nuclear Sclerosis grade 2 or above +/- Posterior Subcapsular Cataract) with mean age of 46.53 yrs. Out of these, we had operated 12 eyes of 10 patients for cataract surgery.

ConjuctivalMicrovasculopathy was seen in 2 patients (3.84%). We observed 3 patients (5.76%) of Blepharitis and 2 patients of Anterior Uveitis.

Table 2:- Anterior Segment & Posterior Segment Disease in relation to CD4 T Cell count:

CD4 T CELL COUNT	Total No. of Patients	Patients with Anterior Segment Disease	Patients with Posterior Segment Disease
≤50	1	0	1
51 - 100	2	2	1
101 - 150	3	1	0
151 - 200	2	1	1
201 - 500	48	27	1
>500	44	16	3
Total	100	47	7

1 patient each of Angle Closure Glaucoma, Oculomotor Nerve Palsy, Ciliary & Intercalary Staphyloma + leucomatous corneal opacity, viral keratitis and Allergic Conjuctivitis was seen.Other Anterior Segment findings include patients with Stye (2 patients) and Pterygium (3 patients)

24 patients (46.15%) with anterior segment disease were having HIV since more than 5 years duration.

In Posterior Segment manifestations,Weobserved 1 patient each of Active CMV Retinitis, RD due to old CMV Retinitis infection and PORN – Progressive Outer Retinal Necrosis. All these patients were having visual acuity HM+/PL+ and below.

2 patients had HIV Retinopathy,BRVO was seen in 1 patient and 1 patient had Macular Scar.

Table 3:- Correlating The Findings With Cd4 Counts:

Ocular Disease	No of Patients	CD4 T Cell Count					
		≤50	51-100	101-150	151-200	201-500	>500
Anterior Segment & Adnexa							
Blepharitis	3	0	0	0	0	1	2
Stye	2	0	0	0	0	0	2
Pterygium	3	0	0	0	0	3	0
Allergic conjuctivitis	1	0	0	0	0	1	0
Conjunctivalmicrovasculopathy	2	0	2	0	0	0	0
Viral keratitis	1	0	0	0	0	1	0
Anterior Uveitis	2	0	0	1	0	0	1
Glaucoma (angle closure)	1	0	0	0	0	0	1
cataract	15	0	0	0	0	8	7
Dry eye	23	0	0	0	1	15	7
Pupil sparing 3rd nerve palsy	1	0	0	0	0	1	0
Ciliary & Intercalary Staphyloma + leucomatous corneal opacity	1	0	0	0	0	1	0
Posterior Segment Disease							
CMV Retinitis	1	1	0	0	0	0	0
PORN	1	0	1	0	0	0	0
Old Retinal Detachment (Post CMV Retinitis)	1	0	0	0	0	0	1
HIV Retinopathy	2	0	0	0	1	0	1
Macular Scar	1	0	0	0	0	1	0
IT-BRVO with Macular Oedema	1	0	0	0	0	0	1

Ocular Findings like Congenital Ptosis, High Myopia with WWOP areas, Multiple Lattice Degenerations, Iris+fundus Coloboma were also observed which were not related to HIV infections.

In this study, only 1 patient was having CD4 T Cell count below 50, which had Posterior Segment disease while out of 2 patients with CD4 T Cell count between 51-100, one had Anterior + Posterior Segment involvement and 1 was having only Anterior Segment disease. So, all patients with CD4 T Cell count below 100 cells/µl were having ocular manifestations.

Majority of patients (91.4%) with Anterior Segment disease were having CD4 T cell count above 200 cells/µl. All patients with Cataract and 95.65% patients with Dry Eye were having CD4 T Cell count above 200cells/µl.

All patients with acute retinal disease (CMV Retinitis & PORN) were having CD4 T Cell count below 100cells/µl.

The average CD4 count in the 28 male patients with ocular manifestations was found to be 498.94 cells/µl and in 24 female patients was 498.38 cells/µl.

The correlation between CD4 T Cell count and occurrence of Anterior- Posterior Segment Disease was clinically significant (p value 0.026).

Discussion:-

AIDS is an infectious disease which lead to slow fall in CD4 T Cell count which increases the risk of opportunistic infections and neoplasia. AIDS is a multisystem disorder and ocular involvement can occur anytime during the natural course of the disease.Recentstudies show that introduction of HAART had changed the pattern of ocular involvement in these patients.

In our study, Anterior Segment manifestations were seen more commonly than Posterior Segment manifestations with Dry Eye being the most common ocular manifestation found.

Occurrence of ocular manifestations was Not found to be significantly affected by Gender and Age of the patients or by the duration of the Disease. (p value >0.05)

We did not observe any patient with HZO, Kaposi Sarcoma, OSSN, Molluscum Contagiosum or with Ocular Toxoplasmosis and Ocular Tuberculosis.

In our study, all patients were on regular HAART therapy. The average CD4 T Cell count in the study population was 506cells/µl. which shows that adherence to treatment regimen help to maintain good immune status and thereby reducing incidence of vision threatening opportunistic infections and neoplasia.

Numerous studies have been carried out to study the prevalence of ocular manifestations in HIV positive patients, which is found to be around 40-70%. [3](Table 4)

Mukta Sharma et al[23] conducted a similar cross-sectional study on 150 confirm HIV positive patients on HAART,51.3% Patients were having CD4 T cell count above 200 cells/µl. They found 4 patients with Severe Dry Eye, 2 patients each of Molluscum Contagiosum and HZO and 5 patients were having Anterior Uveitis. They observed 10 patients with HIV Retinopathy. CMV Retinitis was seen in 2 patients, both having CD4 T Cell count below 50 cells/µl. That correlates low CD4 T cell count as major risk factor in development of CMV Retinitis. They saw 1 patient each of Optic Atrophy and Papilledema,

A Prospective Study on 200 known HIV patients conducted by Saini N et al [24] found Dry Eye as the most common positive finding (41 patients) and HIV Retinopathy (40 patients) as 2nd most common manifestation. 5 cases of CMV Retinitis observed with all patients having CD4 T Cell count below 50 cells/µl. One case each of Ocular Toxoplasmosis and Acute Retinal Necrosis was observed, which are quite rare ocular manifestations. HZO, Molluscum Contagiosum and Uveitis was seen in large number of patients (6, 2 and 10 patients, respectively) in that study.

Table 4:-

Study	No of Patients	Prevalence of ocular manifestations
Mukta Sharma et al (2018)	150	35.3%
Saini N et al (2019)	200	43%
Martin Odoom et al (2016)	100	48%
Young Shin Kim et al (2015)	127	48%
Present study	100	52%

A study conducted by Martin-Odoom et al [25]also showed that occurrence of ocular complications was not significantly related to duration of the disease as well as the gender of the patient.

Young Shin Kim et al [16] found that Anterior Segment Diseases are becoming more common in these patients with Dry Eye having major proportion of patients.

Biswas et al (2000) [12] found CMV retinitis (17%) and HIV retinopathy (15%) as the most common HIV-associated ocular lesions.

According to a study conducted by Sudharshan et al (2013) [22], CMV retinitis was the most common opportunistic infection in HIV patients.

Similarly, a study conducted by Singalavanija T et al [21], revealed that dry eye was the most common anterior segment disorder with the prevalence of 9.9% comparing to the previous report by S. Ausayakhun (2003) which was 2%. [20].

But we had taken only Schirmer 1 Test reading as a diagnostic criterion for Dry Eye, all these patients need to be evaluated according to the Dry Eye Severity Grading Scheme.

Mean age of the 15 patients with Cataract was 46.53 yrs, which suggest early development of cataractous changes. KempenJH et al also found development of cataractous changes at early age in AIDS patients in a study conducted by them.[15]

Anterior segment manifestations were seen with higher CD4 T Cell count, while vision threatening active Posterior Segment diseases were common with low CD4 T Cell count.

Study by Whitcup S et al, also concluded that with the introduction of HAART, the incidence of ocular opportunistic infections causing retinitis, such as cytomegalovirus (CMV), varicella zoster virus (VZV), tuberculosis, and toxoplasmosis, has dramatically decreased.[18]

With HAART, there is a reduction in the number of opportunistic infections, improvement in the length and quality of life; patients are less likely to be blind from posterior segment infections.[17] This longer survival rate may lead to an increased prevalence of the anterior segment and external ocular disorders. Therefore, anterior segment and external ocular disorders become greater concern in the HAART era by affecting the quality of life of infected individuals.

Conclusion:-

AIDS is a multisystem disease, with prevalence of ocular manifestation found to be 52% in our study. Introduction of HAART had significantly improved immune status of these patients, reflected as high CD4 T Cell count and dramatic decrease in occurrence of sight threatening opportunistic infections and neoplasia. Anterior segment diseases are increasing as compared to posterior segment, which causes symptoms of discomfort and irritation, more commonly, rather than vision deterioration. Occurrence of ocular manifestation is independent of age & gender of the patient and duration of the disease.Henceall patients should be screened by ophthalmologist irrespective of symptoms, CD4 T Cell count and Duration of disease. Due to the social stigma associated with this disease, patients hesitate to approach the health care system outside the ART Centre, so a good coordination between ART Centre and other department of the hospital can help in early screening and prompt treatment of this patients and thus reducing ocular morbidity.

Financial support and sponsorship:
Nil.

Conflicts of interest:
There are no conflicts of interest.

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