ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 03 | March - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A STUDY OF OCULAR MANIFESTATIONS IN HIV PATIENTS ON ANTIRETROVIRAL THERAPY (ART)

Ophthalmology

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ABSTRACT

Objective:

- To assess the prevalence of ocular manifestations
- To determine the factors associated with the ocular manifestation like CD4 count and duration of treatment.

Material And Methods: A Hospital based cross sectional analytical study was conducted in the Department of ophthalmology, in a tertiary health care hospital for a period of 18 months from September 2019 to March 2021. A total of 82 patients with HIV on ART attending ART centre of the same hospital of both gender of any age with clinical presentations, diagnosed as HIV and under ART were included in the study. Patients who were not willing to participate were excluded from the study. After obtaining permission from the institution ethics committee and taking informed consent detailed history, clinical examination and investigations were done. Slit lamp examination and fundoscopy were done to assess the ocular manifestations among the eligible patients. Optical Coherence Tomography were done if needed. **Results:** In our study mean age of study participants was 39.5, median duration of treatment was 4 years and ocular manifestations among the the patients wih HIV on ART was 20.7%. Most of patients presented with posterior segment manifestation like retinal hemorrhage with cotton wool spots and papilledema followed by manifestation over lid and adnexa like blepharitis and herpes zoster ophthalmitis and followed by anterior segment manifestation like conjunctivitis and uveitis. We found that the prevalence of ocular manifestation were higher for patients with CD4 ≤200 when compared to the patients with CD4≥ 200. **CONCLUSION:** The prevalence of ocular manifestations among the HIV patients on ART was 20.7%, Posterior segment manifestation is more common. There was significant association for age, duration of treatment, and CD4 count with the occurrence of ophthalmic manifestations.

KEYWORDS

INTRODUCTION

Human immunodeficiency virus (HIV) is a major global public health problem. According to World Health Organization (WHO), there were an estimated 37.7 million [30.2–45.1 million] people living with HIV at the end of 2020, over two thirds of whom (25.4 million) are in the WHO African Region. In 2020, 680 000 people died from HIV-related causes and 1.5 million people acquired HIV.HIV is a retrovirus which replicates in cluster of differentiation 4 (CD4+) lymphocytes. The global prevalence is estimated to be 0.8%.It causes impairment to the human immune system, which leads to immunocompromised conditions and allows for opportunistic infections to invade many organs. Ocular involvement in HIV can be caused by opportunistic infections, vascular abnormalities, neoplasms, neuro-ophthalmic conditions or adverse effects of medications. However, most commonly it occurs due to opportunistic infections and neoplasms. Ocular manifestations are believed to occur among 50% to 75% of people living with HIV (PLHIV) at some point during the course of their illness. The clinical features of the ocular manifestations in HIV differ between countries, especially between high-income and low to middle-income countries. This is because of improved accessibility to healthcare and to antiretroviral therapy (ART), which has shifted the spectrum of the disease from infectious to non-infectious affections. Since the introduction of ART, the incidence of ocular opportunistic infections causing retinitis, such as cytomegalovirus (CMV), varicella zoster virus (VZV), tuberculosis, and toxoplasmosis, has dramatically decreased. However, newer manifestations of known diseases and ocular lesions as a result of adverse drug reactions are being seen. There has also been recognition of new clinical presentations in the form of immune recovery uveitis, which is now a leading cause of severe vision loss in patients with HIV.

Ophthalmic manifestations of HIV may involve anterior segment and posterior segment including various infections and tumours of the periocular tissues, HIV vasculopathy (retinal haemorrhages, cotton-wool spots, microaneurysms, ischaemic maculopathy and telangiectatic vessels), infectious retinopathy or choroidopathy, and rare neoplasms. In addition, the prevalence of HIV-related ocular manifestations increases as CD4+ T cells count decreases. Studies suggest that between 5 to 25% of all HIV patients in developing countries may become blind in their lifetime. Knowledge of the effect of HIV and AIDS on the eye is important, as ocular manifestations may be the primary presentation of the disease which subsequently can be the cause of visual impairment or blindness, which may compromise the quality of life for patients living with HIV and AIDS. If these ocular manifestations are detected at an early stage and treated promptly, it is possible to prevent or minimize the consequences of visual damage. Taking in to consideration of the limited resources in the country, early identification of the ocular manifestations will help in improving the quality of life of the patients. Moreover, studies on the same is sparse in this part of the country and hence this study was conducted among the HIV patients on ART in a tertiary care hospital to determine the prevalence of ocular manifestations and the factors associated with the ocular manifestation.

OBJECTIVES

To assess the prevalence of ocular manifestations
To determine the factors associated with the ocular manifestation like CD4 count and duration of treatment

MATERIALS AND METHODOLOGY

A hospital based cross sectional analytical study was conducted in the department of ophthalmology, in a tertiary health care hospital, for a period of 18 months from September 2019 to March 2020. A total of 82 patients with HIV on ART attending ART centre of the same hospital, of both gender of any age with clinical presentations, diagnosed as HIV and under ART were included in the study. Patients who were not willing to participate were excluded from the study. After obtaining permission from the institution ethics committee and taking informed consent; a detailed history, clinical examination and associated systemic diseases were recorded. Slit lamp examination, direct ophthalmoscopy, indirect ophthalmoscopy using 20D and slit lamp biomicroscopy using 90Dwere done to assess the ocular manifestations among the eligible patients. The baseline investigations done included complete blood count, C reactive protein, RA factor, fasting and post prandial blood sugar levels, HbA1C, lipid profile, coagulation profile and CD4 lymphocyte count. Serologic antibodies for CMV, X-ray- chest, sacroiliac joint, lumbar spine, optical coherence tomography etc were done if needed.

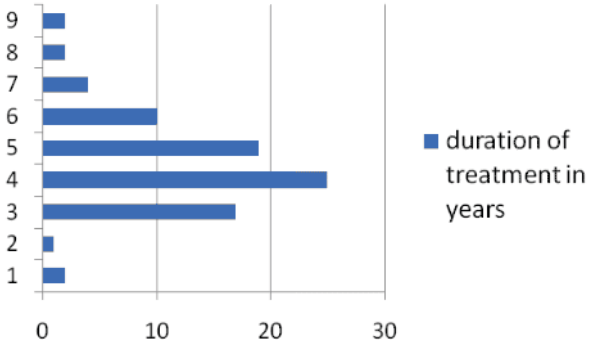
Continuous variables like age, duration of treatment were presented as mean, median depending upon the type of distribution. Categorical variables like gender, associated systemic diseases were presented as frequency and percentages. The data was analysed using SPSS(IBM) Version 21.0 software. Prevalence of ocular manifestations is presented as percentage with 95% confidence interval. Chi-Square test was used to determine the association between the ocular manifestations and associated factors. Independent sample t test was used to determine the association of continuous variables with ocular manifestations. P<0.05 was considered statistically significant. Confidentiality and privacy were maintained.

RESULTS AND OBSERVATIONS

A total of 82 HIV patients on ART were included in the study and the ocular manifestations were recorded. The mean age of the study participants was 39.3 years. The median age of the study participants was 39.5 years with a minimum of 16 years and a maximum of 62 years.

Table No. 1: Shows Gender Distribution Of Study Participants (n=82)

GENDER	FREQUENCY(n)	PERCENTAGE(%)
Male	48	58.5
Female	34	41.5



Bar Diagram 1: Shows The Duration Of Treatment Among The Study Participants(n=82)

The median duration of treatment was 4.0years with a minimum of one year and a maximum of nine years. The mean duration of treatment was4.3 years.

Table No. 2 Shows Prevalence Of Ocular Manifestations Among The Study Participants (n=82)

OCULAR MANIFESTATIONS	FREQUENCY(n)	PERCENTAGE(95%CI)
YES	17	20.7(12.9-31.4)
NO	65	79.3(68.6-87.1)

Table No 3: Shows Site Along With The Type Of Ocular Manifestations Among The Study Participants (n=17)

SITE	FREQUENCY(n)	
LIDS AND ADNEXA	5	3 Blepharitis 2 HZO
ANTERIOR SEGMENT	3	2 Conjunctivitis 1 Uveitis
POSTERIOR SEGEMENT	9	6 Retinal hemorrhage with cotton wool spots 2 Papilloedema 1 CMV retinitis

Table No. 4: Shows Associated Systemic Illness Among The Patients With Ocular Manifestations (n=17)

SYSTEMIC ILLNESS	FREQUENCY
YES	10
NO	7

Of 17 patients with ocular manifestations, associated systemic illness was present among 10 patients. Five patients had hypertension and three patients had diabetes mellitus. Both diabetes and hypertension was present in one patient.rheumatoid arthritis was present in one patient.

Table No. 5: Shows Distribution Of Participants By Cd4 Count(n=82)

CD4 COUNT	PERCENTAGE
<= 200	8.5%
>200	91.5%

Table No. 6: Shows Association Of Duration Of Treatment With The Ocular Manifestations(n=82)

OCULAR MANIFESTATIONS	DURATION OF TREATMENT IN YEARS		P VALUE
	MEAN	SD	
YES	5.6	2.2	0.002
NO	3.9	1.7	

Table No 7 : Shows Association Of Cd4 Count With Ocular Manifestations(n=82)

CD4 COUNT	OCULAR MANIFESTATIONS		P VALUE
	YES	NO	
<=200	6(85.7%)	1(14.3%)	<0.001
>200	11(14.7%)	64(85.3%)	

Table No. 8: Shows Association Of Posterior Ocular Manifestations The Cd4count(n=82)

CD4 COUNT	OCULAR MANIFESTATIONS		P VALUE
	YES(n%)	NO(n%)	
<=200	3(42.9)	4(57.1)	0.005
>200	6(8.0)	69(92.0)	

DISCUSSION

HIV infection causes a wide spectrum of diseases, and ocular manifestations are amongst the most common clinical features. It can manifest in a variety of ways in and around the eyes, and these manifestations vary according to HIV disease severity, specifically, CD4+ T lymphocyte counts. These ocular manifestations can be the presenting sign of a systemic infection of an otherwise asymptomatic individual. The lifetime risk of having at least one abnormal ocular lesion amongst HIV and AIDS individuals ranges from 52% to100%. It is important to explore the burden of ophthalmic manifestations of HIV in our setting for better understanding of the condition which thereby will help in prompt and early management of the condition. Hence this study was conducted among the patients with HIV on ART to determine the prevalence of ophthalmic conditions and the factors associated with it in a tertiary care centre. The mean age of the study participants was 39.3 years in our study with more than half (53.7%) of the study participants in the age group of 31-45 years. Also, more than half (58.5%) were males with a M:F of 1.4:1. A study by Makunyane PSet al also had reported that majority (50.3%) patients belonged to age group of 31-50 years, which is also true with various other studies conducted elsewhere. This needs to be emphasized as the morbidity of these individuals has a considerable impact on the economy of their families. The life time cumulative risk of developing at least one abnormal ocular lesion among HIV positives ranges from 52.0%-100.0%. Our study showed that the prevalence of ocular manifestations among the patients with HIV on ART was 20.7% (95% CI: 12.9%-31.4%). A study by Ghate M et al in India had shown a similar prevalence of ophthalmic manifestations among the patients with HIV on ART. A study by Sharma M et al in Northern part of India had shown a higher prevalence rate of 35.3%, which is in contrast to a

study by Shah SU et al where the prevalence of ocular manifestations in HIV/AIDS patients on ART was 8%. Amsalu A et al in their study in Ethiopia had reported that HIV related ocular manifestation was 14.2%. Evan a study by Bekele S et alin Ethiopia had found that the overall prevalence of ocular manifestations was 25.3%. Other studies in Africa had also shown a lower prevalence rate of ophthalmic manifestations, comparable to our study findings. Narasimhaiah VB et al, however, reported a very high prevalence of 70.0%. Various other studies conducted in India and other parts of the world had reported a varying prevalence. In this era of ART, the prevalence of ophthalmic manifestations have generally showed a declining trend. Agarwal A et alin their study had shown that the prevalence of ocular manifestations was not statistically different in the two eras (38%, in ART era vs 41.67% in pre-ART era). However, this varying prevalence could be attributable to various reasons. The first being the clinics with referral report a relatively higher prevalence and the prevalence also shows variations with the duration of ART and the CD4 count. Accordingly our study showed that the patients with the ocular manifestations had a longer duration of treatment when compared to the patients without the ocular manifestations (5.6 years vs 3.9 years) and it was found to be statistically significant (p=0.002), which indirectly shows that the duration of disease was also longer for these patients and ART is usually started for patients with CD4 less than 250 cells/µl and hence it corresponds to the higher possibility of ocular manifestations. It is also supported by a study finding by Bekele S et al in which the patients who were on ART had a high prevalence of ocular manifestations compared to those who were on ART. This could be due to the low CD4+ T cells count during the initiation of ART as patients with a CD4+ T cell count of <250 cells/µl are put on ART.LowCD4 count is associated with higher prevalence of ocular manifestation as shown in this study and patients might have already developed the manifestation before initiation of ART. The same study showed that the mean CD4+ T cells count of patients with ocular manifestation was lower than the mean CD4+ T cell count of patients without ocular manifestations. Our study also showed that the prevalence of ocular manifestations were higher for patients with CD4 ≤ 200 cells/µl when compared to the patients with CD4 >200 cells/µl (85.7% vs 14.7%) and it was found to be statistically significant (p<0.001). These results are consistent with various other studies conducted elsewhere.

Another finding our study is that out of 17 patients with ocular manifestations, five patients had manifestation over the lids and adnexa (blepharitis in three patients and herpes zoster ophthalmitis in two patients). Of three patients with anterior segment manifestations, two patients had conjunctivitis and one patient had uveitis. Of nine patients with posterior segment manifestations, retinal hemorrhage with cotton wool spots was present in six patients, papilledema was present in two patients and the remaining one patient had CMV retinitis. The prevalence of posterior ocular manifestations were higher for patients with CD4 ≤ 200 when compared to the patients with CD4 >200 (42.9% vs 8.0%) and it was found to be statistically significant (p=0.005). Although, recent studies had shown that in the ART era clinical entities like immune recovery uveitis have appeared as a cause of concern related to blindness, only one case of uveitis was reported in our study. Even a study by Amsalu A et alhad reported only three cases with uveitis in their study. The anterior uveitis is generally believed to be caused by the low immune status of participants, which result in opportunistic infections invading the body and causing inflammatory reactions. Immune recovery uveitis is believed to be a result of a partially restored immune system after the initiation of ART, which mounted an exuberant inflammatory response called immune reconstitution syndrome (IRS). However, our study showed a lesser incidence of uveitis which could be due to the difference in the study population or also could be due to the lesser sample size in our study. Sharma M et al in their study also had observed similar eye manifestation where lid and adnexal manifestations was reported among 7%, anterior segment manifestations was reported in 13.3% and posterior segment manifestations in 14% patients. Agarwal A et alhad reported that cytomegalovirus (CMV) retinitis and HIV retinopathy continued to remain the most common infectious and non-infectious cause of visual morbidity. Even in a study by Amsalu A et al, seborrheic blepharitis (5%) was the most common ocular manifestation, followed by squamoid conjunctival growth (3.8%). Gogri PY et alhad shown that HIV retinopathy was the most common HIV-associated ophthalmic lesion while anterior uveitis was the most common anterior segment finding. The study also showed that the posterior segment lesion was significantly associated with lower CD4 count. Kai S et al had also shown that the most common lesion found was HIV retinopathy found in 9% of patients, followed by CMV retinitis in 6.5%. However posterior segment abnormalities were relatively higher in our patients when compared to a study by GhateM et al, in which the posterior segment lesions were lesser. It is also believed that owing to the current government guidelines of "test and treat" and the newer, more effective regimen in the national program, the incidence of posterior segment manifestations to be lesser contrary to the findings of our study. But these should be interpreted with caution owing to lesser sample size and the different patient characteristics in terms of duration and stage of disease and the CD4 count. One of the limitations of the study is the lesser sample size and hence the issue of generalizability. However, our study results could be extrapolated to patient's similar setting and clinical characteristics. Moreover, the cross-sectional nature of the study had made it difficult to establish the association with the causal factors for the occurrence of ophthalmic manifestations.

To conclude, it has been demonstrated that the CD4+ T-cell count may help to predict the occurrence of ocular manifestations in HIV. Indeed, the risk of developing ocular disease in HIV is increased when the CD4 count is < 200 cells/µL. This is consistent with our findings. Although sufficient care is generally provided, patients often do not adhere to treatment and to follow-up which might be responsible for the opportunistic infections. Hence further research with a larger sample size would help to add robustness to our study findings.

CONCLUSION

The prevalence of ocular manifestations among the patients with HIV on ART was 20.7% (95% CI: 12.9%-31.4%). Out of 17 patients with ocular manifestations, five patients had manifestation over the lids and adnexa (blepharitis in three patients and herpes zoster ophthalmitis in two patients). Anterior segment and posterior segment manifestations were noticed among three and nine patients respectively. Of three patients with anterior segment manifestations, two patients had conjunctivitis and one patient had uveitis. Of nine patients with posterior segment manifestations, retinal hemorrhage with cotton wool spots was present in six patients, papilledema was present in two patients and the remaining one patient had CMV retinitis.

There was a significant association for age, duration of treatment and CD4 count with the occurrence of ophthalmic manifestations. The prevalence of posterior ocular manifestations were higher for patients with CD4 ≤ 200 when compared to the patients with CD4 >200 (42.9% vs 8.0%) and it was found to be statistically significant (p=0.005). Further research with a larger sample size would help to add robustness to our study findings.

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