

CLINICAL STUDY OF FUNDAL CHANGES IN HIV/AIDS AND ITS CORRELATION WITH CD4+T CELLS IN PATIENTS ATTENDING A.R.T. CENTRE OF I.G.I.M.S.



Ophthalmology

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ABSTRACT

Background: Human immunodeficiency virus (HIV) infection and Acquired Immuno-Deficiency Syndrome (AIDS) is a global pandemic. Study aimed to record the retinal manifestations in patients with HIV according to their CD4+ count and HAART status.

Conclusion: There is higher incidence of retinal findings in non-HAART group and in patients with CD4+.

KEYWORDS

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is now a global pandemic with more than 40 million people in the world being affected causing enormous human, social and economic toll in the world. It is a morbid condition characterised by severe impairment of the immune system with the onset of a number of opportunistic infections and tumours. The etiology is human deficiency virus (HIV) a retrovirus with elective tropism for the T-HELPER lymphocytes Cd4+.

The virus infects the T-lymphocytes leading to selective loss of CD4+T cells resulting in profound immunodeficiency. This progressive damage of human host is the harbinger of opportunistic infection and neoplasms which are the main cause of morbidity and mortality in AIDS.

The posterior segment of the eye is predisposed to disorders that involve the retina, choroid and optic nerve in HIV infection. The ocular posterior segment manifestations of AIDS may be divided into four categories: retinal vasculopathy, unusual malignancies, neuro-ophthalmologic abnormalities, and opportunistic infections. The majority of cases of retinal disease are seen in severely immunocompromised individuals, with CD4+ counts of less than or equal to 100 cells/mm³.

HIV retinopathy, also referred to as HIV-related ocular micro-angiopathic syndrome, is a non-infectious microvascular disorder characterised by cotton wool spots, microaneurysms, retinal haemorrhages, Roth spots, telangiectatic vascular changes and areas of capillary non-perfusion. HIV retinopathy is one of the most common retinal manifestations of HIV and is found in 70% of persons with HIV/AIDS.

The severity of ophthalmic complications of HIV infection increase as immunodeficiency decreases which is measured by CD4+Tcells count. Most importantly, ocular signs and retinal manifestations of AIDS patients occur in 10-20% of cases in CMV retinitis.

Epidemiology:

Since the beginning of the epidemic, almost 78 million people have been infected with the HIV virus and about 39 million people have died of HIV. Globally, 35.0 million [33.2–37.2 million] people were living with HIV at the end of 2013. An estimated 0.8% of adults aged 15–49 years worldwide are living with HIV, although the burden of the epidemic continues to vary considerably between countries and regions. While the National AIDS Control Organisation estimated that 2.39 million people live with HIV/AIDS in India in 2008–09, a more recent investigation by the Million Death Study Collaborators in the British Medical Journal (2010) estimates the population to be between 1.4–1.6 million people.

Thus, the present study is undertaken to study of FUNDAL

CHANGES in HIV/AIDS patients and also to determine the relationship between FUNDAL CHANGES in HIV infection and its correlation with the degree of immunodeficiency as measured by CD4+T cell count.

OBJECTIVES

- To study FUNDAL CHANGES in HIV/AIDS patients.
- To study the relationship between FUNDAL CHANGES in HIV infection and the degree of immunodeficiency as measured by CD4+Tcell count.

MATERIALS AND METHODS

The present study titled 'CLINICAL STUDY OF FUNDAL CHANGES IN HIV/AIDS AND ITS CORRELATION WITH CD4+T CELLS IN PATIENTS ATTENDING A.R.T. CENTRE OF I.G.I.M.S.' was conducted in Department of Ophthalmology, Indira Gandhi Institute of Medical Science, Patna.

Study design

A prospective study.

Method of collection of data

Source of Data

Patients known to be positive for HIV infection with or without AIDS being referred from the A.R.T. Centre of I.G.I.M.S., on treatment/without treatment, and have determined their CD4+T lymphocyte cell count, belonging to any age and of either gender at Department of Ophthalmology, were enrolled in this study.

Sample size

A sample size of 100 cases was taken.

SELECTION CRITERIA

INCLUSION CRITERIA

- All the patients who are seropositive to HIV.
- Seropositive HIV patients with or without AIDS.
- Seropositive HIV patients in whom CD4+Tcell count has been determined

EXCLUSION CRITERIA

- Patients who are not compliant or is not willing to give consent for examination.
- Patients with similar ocular manifestation secondary to immunosuppression due to other causes including tuberculosis.

METHODOLOGY

After obtaining the informed consent, patients were enrolled in the study. Detailed evaluation of the patient including a detailed history by personal interrogation either with the patient or his/her relative, was noted. Emphasis was given to elicit history of high risk behaviour, blood transfusion, intravenous drug abuse and other habits. Family history, status of the spouse if married and children if present, weather

dead or alive and the cause of death were noted. History regarding ocular complaints was enquired in detail.

The relevant treatment for ocular complaints was instituted, along with the consultation with the physician for systemic condition, when required.

Main parameters studied :

- The FUNDAL CHANGES in HIV/AIDS patients.
- The relationship between FUNDAL CHANGES in HIV infection and the degree of immunodeficiency as measured by CD4+Tcell count.

STATISTICAL ANALYSIS:

- FUNDAL CHANGES in HIV/AIDS was determined as the percentage of the total patients examined, having posterior segment manifestations of HIV/AIDS.
- Association between ocular manifestations of HIV/AIDS & CD4+T cell count was analysed using Chi- square test.

RESULTS

The present study was conducted on 100 HIV positive patients with or without AIDS, on treatment or not, who presented or were referred to the Ophthalmology Out Patient Department at Indira Gandhi Institute of Medical Science, Patna. The patients who had their CD4+ T lymphocyte count were enrolled in the study. The fundal changes in HIV/AIDS patients and its correlation with CD4+ T cell count studied. The data was tabulated as follows :

Table 1: Age And Sex Distribution Of Patients Studied (n=100)

Sl. No.	Age group (years)	Total Number of patients	Male	Female
1	0-9	7	2	5
2	10-19*	-	-	-
3	20-29	12	4	8
4	30-39	42	27	15
5	40-49	29	18	11
6	50-59	7	6	1
7	60-69	3	1	2
8	Total	100	58	42

* No patients enrolled in the study were in this age group.

In our study, the mean age of the patients was found to be 36.4 years ranging from 1 year 3 months to 68 years with a SD of 11.6 years.

Majority of patients, i.e. 42(42%) were within the age group of 30- 39 years.

The no. of males studied were 58(58%) and the no. of females were 42 (42%). The majority of males i.e., 27 were in the age group of 30- 39 years and the majority of females i.e. 15 were also in the age group of 30- 39 years.

Graph 1 : Age And Sex Distribution Of Patients Studied

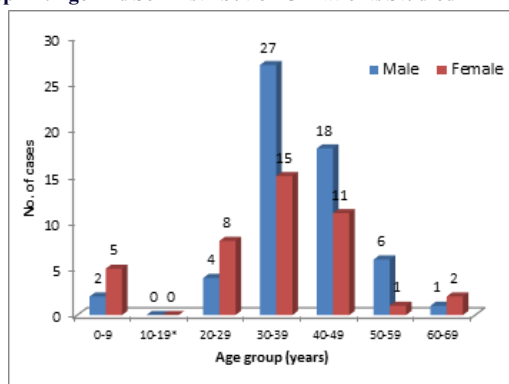
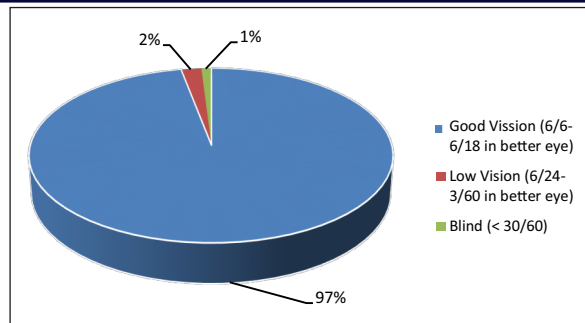


Table 2 : Visual Status In Hiv / Aids Patients :

Serial No.	1	2	3
Condition	Good Vission (6/6-6/18 in better eye)	Low Vission (6/24-3/60 in better eye)	Blind (< 30/60)
Total No. of patients	97%	2%	1%



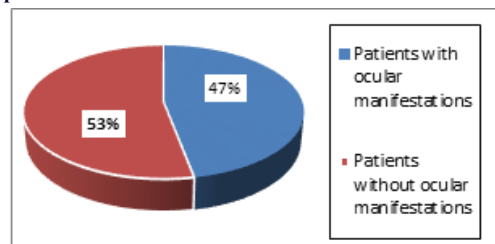
Graph 2 : Visual Status In Hiv / Aids Patients :

Table 3: Ocular Manifestations In Hiv / Aids (n = 100)

Serial No.	1	2
Condition	Patients with ocular manifestations	Patients without ocular manifestations
Total No. of patients	47%	53%

Our study showed the prevalence of ocular manifestations among HIV positive patients as 47%.

Graph 3: Ocular Manifestations In Hiv / Aids



DISCUSSION

The present study was conducted on 100 patients who were known to be positive for HIV infection with or without AIDS on treatment / without treatment, and have determined their CD4+T lymphocyte cell count, at Department of Ophthalmology, Indira Gandhi Institute of Medical Science, Patna.

I: SOCIO-DEMOGRAPHIC CHARACTERISTICS OF STUDY PARTICIPANTS:

Age and sex distribution of patients studied:- In the present study the mean age of the participants was 36.4 years. Majority i.e. 42 (42%) participants were in the age group of 30- 39 years. 58(58%) patients were males and 42 (42%) patients were females. The majority of males i.e. 27 and the majority of females i.e. 15 were in the age group of 30- 39 years. Cochereau I et al in a study in Africa in 1999 have found the mean age of 37 years.

In this series the highest prevalence is in the 4th and 5th decade with the mean age of 36.4 years. The present study, in accordance with the previous studies has a similar pattern of age distribution but shows an almost equal to higher infection rate in males (58% compared to 42% in females). This change in trend may be due to higher awareness among people towards HIV infection and AIDS and the mandatory testing of the spouses of infected males on registration to the ART centers recognized by NACO.

Distribution of cases by mode of transmission:-

The present study shows the most common risk of exposure is sexual route which is observed in 81 (81 %) participants, of which only two people acquired the infection by homosexual route, the rest having acquired the infection by heterosexual contact. Seven children (age 0-9 years) had acquired the infection perinatally and in 1 (1%) patient the mode of acquiring infection could possibly be traced to blood transfusion. Rest of the 11% denied revealing the route of infection.

III. OCULAR MANIFESTATIONS:

The visual status in HIV/AIDS patients:

In our study, 97 (97%) patients had good vision (6/6 –6/18 in the better eye), 2 (2%) patients had low vision (6/24 –3/60 in the better eye) attributable to cataract and 1 (1%) patient was blind (as classified by WHO). 31 (31%) patients had uncorrected refractive error. The

percentage of one eyed patients in our study was 7%. Three patients had only perception of light in one eye, attributable to retinal detachment secondary to Cytomegalovirus retinitis in 2 and orbital cellulitis following lid abscess in 1 patient. Biswas J et al have reported that in due course of the disease process, visual acuity worsened in 9 eyes of the 163 eyes due to various ocular lesions.¹⁰⁷

In our study majority i.e. 97 (97%) had good vision. This shows that diminution of vision is rarely complained of by the patients suffering from HIV infection because of the good vision in the better eye. So visual acuity cannot be taken as the indicator of the ophthalmic manifestation. Routine screening is the only way to detect the ophthalmic manifestations of HIV infection.

Percentage of patients with ocular manifestations :-

In our study the ocular manifestations of HIV/AIDS was found in 47(47%) patients. Lewallen S in a study of 99 patients with AIDS reported that 26% of the patients had abnormal ocular findings and rest 73 % had normal ocular examination.⁸⁴ A study done in Africa by Cochereau I et al reported the prevalence of AIDS related eye diseases in 21% of the patients.

Our study shows results comparable with the study in Chennai⁶. The prevalence is well within the range of 50- 100% life time cumulative risk as quoted by Kestelyn PG et al.

Ocular manifestations in HIV/AIDS patients:-

Posterior segment manifestations in HIV :-

HIV Retinopathy:

In the present study, 14 (14%) patients had HIV retinopathy as the most common ocular finding. Of these 14 patients, 11(78.5%) had cotton wool spots (CWS) i.e. 9 having only CWS and 2 having both CWS and dot haemorrhages. 3 (25%) patients had retinal hemorrhages only in the form of flame shaped and dot haemorrhages. No patient had visual impairment attributable to HIV retinopathy. Jabs DA found that the prevalence of non - infectious retinal microangiopathy in HIV infection was 50%. Sahu et al reported that 34.2% of HIV infected patients had HIV- retinopathy, among a cohort of south Indian patients, making it the most common ocular manifestation in HIV/AIDS.

Our findings are consistent with the other studies in which HIV retinopathy is the most common ocular manifestation of HIV/AIDS. These are usually asymptomatic and thus can be missed unless looked for specifically in HIV infected patients. It is proved that in absence of Diabetes mellitus and Hypertension, presence of even a single CWS in an otherwise normal fundus is suggestive of HIV infection.

CMV Retinitis:

In the present study Cytomegalovirus retinitis was found in 5 patients (5%) with one patient returning to us with Immune Recovery Uveitis after 8 months of initial diagnosis of indolent CMV retinitis.

Holland et al observed that the introduction of HAART has markedly reduced the incidence of CMV retinitis, but has not eliminated new cases all together. Jabs DA has reported a cumulative probability of a retinal detachment in atleast one eye of 57% at 12 months after diagnosis of CMV retinitis. Banker AS et al showed 41.7% incidence of IRV in a cohort of Indian patients.

Neuro-ophthalmic manifestations:

In our study 5(5%) patients had neurological abnormalities. They included papilledema in 4(4%) patient and cranial nerve palsies in all 1 (1%) patients. Hong Y J et al reported complete binocular blindness as the first manifestation of HIV related cryptococcal meningitis which was also seen in our study in one patient.

Karna et al reported a case of multiple cranial nerves (sixth, ninth, tenth and twelfth nerve) palsy in a HIV positive patient.¹¹⁸ Mwanza J C et al reported 60 % abnormal neuro- ophthalmological disorder in HIV infected subjects with neurological manifestation. Biswas et al reported optic atrophy in 7% and gaze palsy in 1% patient in a study on ocular lesions in HIV- positive cases.

Other posterior segment manifestations:

Other posterior segment manifestations in our study included ARN in 1(1%) patient, Toxoplasmicretino- choroiditis in 1(1%) patient, 6(6%) case of central retinal vein occlusion. Cochereau et al has reported viral retinitis in 1% of the patients in a study in Africa.

Anterior segment manifestations of HIV:-

Our study showed comparatively less occurrence of adnexal and anterior segment manifestations as compared to the posterior segment findings in HIV/AIDS. In the present study Molluscum contagiosum of the eye lids was found in 1(1%) patient. Anterior uveitis was seen in 3 patients (3%). One patient with a lid abscess developed orbital cellulitis rapidly.

Thus, our series, in keeping with other similar studies, shows anterior segment findings are less frequent than the posterior segment findings in HIV/AIDS.

Association between clinical stage of HIV disease (according to WHO) and eye involvement:-

In the present study, majority of the patients i.e. 62 (62%) patients belonged to WHO clinical stage 1 and 2. Thirty eight percent (38%) patients belonged to clinical stage 3 and 4. Three patients (14.2%) in stage 1 and 15 patients (36.6%) in stage 2 disease had ocular lesions. Fifteen patients (65.2%) in stage 3 and 4 patients (93.3%) in stage 4 had ocular lesions. Chi - square analysis showed that the prevalence of ophthalmic manifestations associated with HIV was significantly higher in those with WHO clinical stages 3 or 4(p value <0.05).

Our study showed that prevalence of ocular lesions associated with HIV was significantly higher in patients belonging to WHO clinical stages 3 or 4 and is comparable with other previous studies. Thus, WHO clinical stage may be an important predictor of the presence of ophthalmic manifestations of HIV.

Association between CD 4 + T cell counts and Fundal changes in HIV:

In our study, the majority of patients with ocular manifestations i.e. 12 had CD4 + T cell counts <100 cells/ μ l. Rest of the patients had CD4+ T cell count between 100 and 500 cells/ μ l and only 1 patient (7.1%) had CD 4+ T cell count >400 cells/ μ l. Chi square analysis of the data revealed p value of 0.012 which is highly significant.

In our study we found a significant association between ocular manifestations and lower CD4+ T cell count (0- 100 cells/ μ l) in accordance with other previous studies.

CONCLUSION

The present study is a hospital based prospective study representing the patients with HIV

Strengths of the study:

- All the patients had CD4+ T cell counts done by a standard method single platform flow cytometry using CyFlow system by Partec.
- All the patients underwent a comprehensive ophthalmic examination irrespective of the visual complaints.

Limitations of the study:

- The limited sample size, broad spectrum of diseases, follow - up of selective cases, a lack of control group for comparison and clinical diagnosis of fundal changes are a few limitations of the present study.
- All the pathologies in the fundus was diagnosed clinically.

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