Original Article

Study of prevalence of ocular manifestations in HIV positive patients

Nishtha Saini[1], Sonia Hasija[2], Prempal Kaur[3], Manpreet Kaur[1], Vishal Pathania[4], Ajeet Singh[5]

[1]Department of Ophthalmology, SHKM, GMC Nalhar, Nuh
[2]Department of Pathology, SHKM, GMC Nalhar, Nuh
[3]Department of Ophthalmology, GMC Amritsar
[4]Department of ENT, SGT Medical college, Gurgaon
[5]Department of Critical Care Medicine, Medanta- The Medicity

Abstract

Introduction: HIV/AIDS is a disorder which affects multiple systems in our body but ophthalmic manifestations do occur in 70-80% of patients sometime during their lifetime. Eye is affected either directly by HIV virus or indirectly through various opportunistic infections. HIV related ophthalmic manifestations are wide and can affect any part of eye from adnexal disorders to posterior segment diseases including the optic nerve and the optic tract. This study was done to know the prevalence of ocular manifestations in the known HIV positive case & to correlate the ocular manifestations in HIV positive patients with their CD4+ lymphocyte count and duration of disease.

Material & Methods: In the present study, we examined 200 known cases of HIV infection who attended the Out Patient Department of Government Eye Hospital, Amritsar, Punjab. Detailed ocular examination was done and the findings were correlated with CD4 + count and duration of the disease.

Result: In the present study it was found that dry eye and HIV retinopathy were amongst the most common ocular manifestations accounting for 20.5% and 20% of the total cases. Next in the series was neuro ophthalmic complications which included papilledema, optic nerve atrophy, papillitis and also third nerve abnormalities. It consisted of 5.5% of the total cases. Almost equal in incidence was anterior uveitis consisting of 5% of the total. Next of importance was CMV retinitis of which 5 cases were seen which constituted 2.5% of the total and all these cases were observed in the patients with CD4+ count less than 50/mm3. p value for this was 0.008 which was statistically significant. Few cases of blepharitis, conjunctivitis, cellulitis, herpes zoster ophthalmicus and keratitis were also found which consisted of 2.5%, 0.5%, 1%, 3%, and 2% respectively.

Conclusion: Any HIV-infected person who at any stage experiences ocular symptoms also should get competent ophthalmologic care at the earliest. Any delay in treatment can lead to permanent visual loss. An improved coordination between two branches of ophthalmology and HIV medicine will need long coordination against this dreadful disease.

Key words: HIV/AIDS, ophthalmic manifestations, optic nerve, posterior segment diseases

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Corresponding author
Dr. Sonia Hasija
Assistant Professor, Department of Pathology
SHKM GMC Nalhar Nuh 221107
Contact no: 9728141421
E-mail: drsoniahasija@gmail.com

Introduction

Human immunodeficiency virus (HIV) causes Acquired Immune Deficiency Syndrome (AIDS), one of the most dreadful infectious diseases of the present time. It has made a significant effect on modern medicine, public health priorities and our modern society. At the beginning of the 20th century, Sir William Osler said, if one knows Syphilis, one knows medicine. Now a days it implies to AIDS. The virus infects the T-lymphocytes, resulting in profound immunodeficiency leading to opportunistic infections and neoplasms.(Rao, 1994)

Eye is affected in more than 70% of HIV positive patients with HIV infection sometime during the natural history of their infection. (Cunningham et al, 1998) HIV can affect the eye either directly or indirectly by means of various opportunistic infections. The spectrum of HIV-associated ophthalmic manifestations are diverse and can affect any part of eye from adnexal disorders to posterior segment diseases including the optic nerve even upto the optic tract.(Rajeev Soman et al, 2008)

The manifestations of this infection can affect both the anterior or posterior segment of the eye. The spectrum of anterior segment disease include tumours of the periocular tissues and a variety of external infections. Posterior segment manifestations include an HIV-associated retinopathy and a number of opportunistic infections of the retina and choroid. The increase in life span of HIV positive people has resulted in more patients being affected with oppurtunistic infections of the retina. Luckily, most of such infections respond well to medicines. So it is really important to recognize and treat these infections at the earliest.

Material and Methods

The present prospective study was carried out in Department of Ophthalmology, Ram Lal Eye Hospital attached to Government Medical College, Amritsar, Punjab. Diagnosed HIV positive patients was included in the study irrespective of taking any consideration of age, sex, work and duration of illness. Information of patients was kept confidential except for publication purposes. Patients with other immunodeficiency disorders were excluded from the study.

A total of 200 known HIV infection patients were studied over a period of two years, who were known cases of HIV infection. For the confirmation of laboratory diagnosis of HIV, serum sample was considered positive only if it was found to be reactive by rapid enzyme immunoassays. Diagnosis was confirmed by Enzyme-Linked Immunosorbent Assay (ELISA). Western Blot was not done as it was not available in our hospital. CD 4+ lymphocyte count was routinely done as the findings were co-related with the CD4+lymphocyte count. The selected cases were subjected to detailed and comprehensive ocular examination. Both the eyes of the patients were meticulously examined. The various steps of the ophthalmic examination included:

1. IOP was recorded with Schiotz tonometer after every examination
2. Complete examination of the orbit
3. All ocular movements were checked to see for any cranial nerve involvement
4. Complete external examination of the eye was performed
5. Anterior segment examination was done both in diffuse light and also by the slit lamp biomicroscopy (AIA - 11 Dynamic)
6. Visual acuity of both the eyes was checked.
7. Schirmer test (I & II) and examination of lacrimal apparatus of the eyes was done to look for dry eye or any other problem.
8. Detailed fundus examination by both direct (90 D, 78 D) and indirect ophthalmoscopy (20D) was also done. The examination was done after dilating the pupil with 10%

phenylephrine, 1% tropicamide drops. One drop of the medicine was instilled in both the eyes at an interval of ten minutes, for three times.

9. Detailed facial nerve examination was also done.

   Ocular manifestations were compared according to the CD4+ count and the duration of the disease. Depending on the CD4+ count comparison was done as follows:

   Group 1: CD4+ count > 500/mm3
   Group 2: CD4+ count: 201-500/mm3
   Group 3: CD4+ count: 101-200/mm3
   Group 4: CD4+ count: 50-100/mm3
   Group 5: CD4+ count: <50/mm3

   Comparison was also done depending on the duration of the disease. Depending upon duration comparison was done as follows:

   Group 1: Duration < 1 year
   Group 2: Duration > 1 year

All the patients were examined in the above mentioned manner and baseline data was recorded in the proforma. Proforma also included the results of the following investigations

i. ELISA
ii. Rapid Enzyme Immunoassays
iii. CD 4+ Lymphocyte count

All the findings were recorded in tabulated form and various relationships were studied. Prevalence of ocular manifestations was studied in the HIV positive individuals and their co-relation was found with CD 4+ lymphocyte count and the duration of the disease. Actually we could not find exact duration of disease, it was taken as duration since the HIV infection was diagnosed. All parameters were not only tabulated but also analyzed by using suitable statistical tests.

Results

The commonest age group affected in the study was 31-40 years which had total 96 patients which comprised of 48% of the total patients. In this study 132 males & 68 females were included. In the present study 81.5% patients got the disease through sexual route, 8.5% gave history of intravenous & substance abuse injections, 9% got the disease through contaminated blood transfusion and 11% got the disease through perinatal transmission. In the present study only 12% of the cases were single and remaining 88% married. Among the married cases 68.5% cases had their spouses reactive for the disease and 17% spouses were non reactive. For the remaining 2.5% spouses, status could not be known as spouses were either separated or had expired. Among the HIV infected males, the majority were majorities were drivers and among females, majority were housewives.

The mean IOP in the study population was found to be 11.79 ± 2.05 mm Hg in the right eye and 11.85 ± 1.98 mm Hg in the left eye. The average for both the eyes was 11.82 ± 1.93 mm Hg. So the mean IOP done by Schizont & non contact tonometery was lower in patients of HIV as compared to normal population confirmed by Applanation Tonometry. The mean reading of Schirmer test was found to be 16.22 ± 5.66 mm.

In the present study 200 HIV positive cases were examined for various ophthalmic manifestations. Out of 200 cases 86 cases (43%) had ophthalmic manifestations when they were examined by an Ophthalmologist.

In our study maximum number of HIV positive patients had dry eye. Forty one patients had dry eye. It was followed by HIV retinopathy, nearly 40 patients suffered from it. Both these manifestations were present in all the CD4 + groups but maximum number was present in the

group with CD4 + count below 50/mm3. Ten patients in the study group also suffered from anterior uveitis. Herpes zoster ophthalmicus was also observed in total 6 patients in the study group. 5 cases of CMV retinitis were also observed and all these cases had CD4 + count below 50. Even ocular toxoplasmosis and acute retinal necrosis which are very rare ophthalmic manifestations were also observed. 1 case each of ocular toxoplasmosis and acute retinal necrosis was observed. 2 cases of central retinal vein occlusion were also seen in the study group which had CD4+ count below 50/ mm3. (Table no 1 & 2)

Table 1: Prevalence of Ocular Manifestations In HIV Positive Patients

S.No.	Diagnosis	No. of patients (out of total 200)	% of the total
1	Blepharitis	5	2.5
2	Neuro- ophthalmic complications	11	5.5
3	HIV retinopathy	40	20
4	Dry eye	41	20.5
5	Conjunctivitis	1	0.5
6	Cellulitis	2	1
7	Uveitis	10	5
8	Herpes Zoster ophthalmicus	6	3
9	Keratitis	4	2
10	Molluscum contagiosum	2	1
11	CMV retinitis	5	2.5
12	Ocular toxoplasmosis	1	0.5
13	CRVO	2	1
14	Acute retinal necrosis	1	0.5

Table 2: Distribution of Various Ocular Manifestations According to the CD4+ Count

Diagnosis	CD 4+ Count (/ mm^3)					
	<50	50-100	100-200	200-500	>500	Total
	No. of patients					
Blepharitis	2	1	0	0	2	5
Neuro ophthalmic complications	4	2	3	1	1	11
HIV retinopathy	14	8	8	8	2	40
Dry eye	9	7	5	5	2	28
Conjunctivitis	0	0	0	0	1	1
Cellulitis	1	0	1	0	0	2
Uveitis	5	3	2	0	0	10
Herpes Zoster Ophthalmicus	3	3	0	0	0	6
Keratitis	3	1	0	0	0	4
Molluscum Contagiosum	2	0	0	0	0	2
CMV Retinitis	5	0	0	0	0	5
Toxoplasmosis	1	0	0	0	0	1
CRVO	2	0	0	0	0	2
ARN	1	0	0	0	0	1
Total	**52**	**25**	**19**	**14**	**8**	**118**

Discussion

AIDS is an infectious disease caused by the slow fall in CD4+ T lymphocytes affects the patients by causing subsequent opportunistic infections and neoplasia. Gradually with deterioration of CD4+ count, the immune system further weakens and symptoms such as malaise, night sweats, fever and cachexia start developing as the infection progresses. Measuring the absolute CD4+ count is an essential part of the staging the disease. No doubts HIV/AIDS is a multisystem disorder but ophthalmic diseases can affect patients with HIV infection anytime during the natural history of their infection. Numerous studies have been carried out to study the prevalence of ocular manifestations in HIV positive cases.

In the present study, we found ocular manifestations in 43% of the patients. Some patients were symptomatic while others were not even aware of the problems they were having. Various studies have been conducted to find ocular manifestations in HIV+ patients, I am mentioning some of these.

Biswas et al (1999) found that during the natural course of HIV, 70-80% of patients do manifest ocular symptomatology. Cunnigham et al (1998) and his co workers studied that 40-45% of HIV-infected patients have one or other ophthalmic manifestations when seen by an ophthalmologist. Phillippe et al (2001) in their study concluded that 50-75% of the HIV infected cases they examined had one or the other ocular manifestations. Narang et al (2004) observed eye diseases in 35% of the HIV+ cases. Figure for Gharai et al (2008) and Assefa et al (2006) are 45% and 60% respectively. Atilli et al (2000) found ocular diseases in 19% of their cases.

Some of the studies found out that lifetime cumulative risk of at least one abnormal ocular lesion in patients of HIV ranges from 52%-100%. (Rao, 1994; Biswas et al, 1999; Biswas et al, 2000; Freeman, 1989)

% Prevalence of occurrence of ocular manifestation according to various studies

Study	% prevalence of ocular manifestations
Present	43
Narang et al (2004)	35
Phillippe et al (2001)	50-75
Gharai et al (2008)	45
Assefa et al (2006)	60
Attili et al (2000)	19
Cunnigham et al (1998)	40-45
Biswas et al (1999)	70-80 (during natural history of the infection)

In the present study it was found that dry eye and HIV retinopathy were amongst the most common ocular manifestations accounting for 20.5% and 20% of the total cases. Next in the series was neuro ophthalmic complications which included papilledema, optic nerve atrophy, papillitis and also third nerve abnormalities. It consisted of 5.5%of the total cases. Almost equal in incidence was anterior uveitis (non granulomatous & bilateral) consisting of 5% of the total. Next of importance was CMV retinitis of which 5 cases were seen which constituted 2.5% of the total and all these cases were observed in the patients with CD4+ count less than 50/ mm3. p value for this was 0.008 which was statistically significant. We also observed that the ocular manifestations were more common in the patients with lower CD4+ count. Lower the CD4+ count, more virulent the disease and more are the chances of ocular manifestations.

Some manifestations like CMV retinitis, ocular toxoplasmosis, CRVO and ARN were only present in patients with CD4+ count below 50/ mm3 while other manifestations were more common in this group. Similarly we also studied the manifestations according to duration of disease but we did not get any correlation as we could get duration of diagnosis but not duration

of disease. This problem arose because of long window period of AIDS and it was also found to be statistically insignificant.

Banker observed that HIV retinopathy was the most common ocular manifestations of posterior segment of the eye in 40-60% of the HIV+ cases. CMV retinitis presented in 40-50% of the patients prior to introduction of HAART but now its incidence has reduced dramatically. He observed neuro ophthalmic complications in 6% cases while ARN, ocular toxoplasmosis, large vessel disease CRVO and BRVO were rare presenting in less than 1% cases. Biswas and Sudharshan studied the anterior segment findings in HIV+ cases and found dry eye was the most common anterior segment finding occurring in 20-38.8% cases. They also found herpes zoster ophthalmicus in 10-20% cases, molluscum contagiosum in 5% cases, Kaposi sarcoma in 10-20% cases and lymphomas in 3.5-5% cases. They observed keratitis, conjunctivitis, blepharitis, cellulitis and lid abscesses in very rare cases, each in less than 1% cases. (Biswas et al, 2008). We did not observe any case of Kaposi sarcoma, lymphoma and lid abscess.

In one of the studies by Jabs DA (1995), it was again shown that most common eye disease i.e. HIV retinopathy, occuring in 50% of the patients with AIDS, 34% of the patients with ARC, and 3% of the patients with asymptomatic HIV infection

Most common opportunistic ocular infection is Cytomegalovirus (CMV) retinitis. It affects around 37% of the patients suffering with AIDS. The lesser common secondary ocular infections includes ocular toxoplasmosis, herpes zoster retinitis, and Pneumocystis choroidopathy, each occurring in < or = 1% of the patients with AIDS. Neuro-ophthalmic lesions were more common and present in 6% of the patients with AIDS (Jabs, 1995). According to Gharai et al, 2008 the most common of the ocular manifestation cytomegalovirus (CMV) retinitis which occurred in 20% of the patients

HIV retinopathy was seen in 11% patients. Other lesions included uveitis (5%), acute retinal necrosis (ARN) (3%), choroiditis (2%), neuro-ophthalmic manifestations (12%), complicated cataract (6%), keratouveitis (1%) and corneal ulcer(1%). (Biswas, 1999) In another study by Sahu and his colleagues CMV retinitis was found in 39.5% and HIV retinopathy in 34% cases of HIV. (Sahu et al, 1999)

Assefa et al in their study found HIV retinopathy in 24%, neuro ophthalmic complications in 9.6%, uveitis in 9%, herpes zoster ophthalmicus in 6% and conjunctivitis in 1% of the patients. They contrary to all other studies found CMV retinitis in less than 1% cases. They explained this remarkable difference by the higher rate of early mortality in African patients. Also, African people have a tendency to spend their last days when they are in their critical conditions at home (Cochereau, 1999; Beare, 2008). moreover, different subtypes of HIV viruses and variations in the race along with co- morbid disease can also be cause of less number of CMV retinitis in the developing part of the world.

Atilli et al, 2008 found the spectrum of lesions with HIV in India different to that from other parts of world. They found HIV retinopathy (54%), blepharitis (34%), papilledema (36%), conjunctivitis (12%), molluscum contagiosum (6%) and CMV(1%) in the HIV+ cases. In one of the studies in Thailand, it was found that fundus abnormalities were present in 28% of the patients, most of them were cotton wool spots and retinal hemorrhages. Even the patients presented with the chief complaints of decreased vision, red eyes and diplopia which were due to retinitis, choroiditis, optic neuropathy, etc. These were less common than the former (Tanterdtam et al, 2000)

In another study in HIV/AIDS patients who

were taking HAART therapy was only 8%. The patients who had visual impairment were around 7%. Mainly the ocular diseases included was HIV retinopathy(5%). Immune recovery uveitis & vitritis were seen in 3% cases each. Higher prevalence of ocular manifestations and visual loss were higher with the CD4 count of 0-100/ mm3. It was also observed that prevalence of ocular manifestation has decreased with introduction of HAART therapy. CD4 count may help predict their occurrence. (Shah et al, 2009) Various studies have shown that with the introduction of HAART therapy, the CD4 count increases and CMV retinitis incidence decreases (Jacobson, 1998; Reed et al, 1997)

Conclusion

AIDS, a multisystem disorder, does affect 70-80% of patients with HIV infection with ocular manifestations. These ocular manifestations should be ruled out by coordination between physician and ophthalmologist before start of antiretroviral drugs. Due to the poor visual prognosis and rapid spread of undiagnosed ophthalmic problems. Due to vision loss & retinal opportunistic infections, all HIV positive disease patients should go for baseline ophthalmologic examination. All patients of HIV-infected viruses whom experiences ocular symptoms also need competent ophthalmologic care at the earliest to prevent irreversible visual loss.

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