Ophthalmic Manifestations in HIV Positive patients and the Indian Perspective

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Abstract

The Eye is a vital sense organ and much like any other organ in the body can be affected by HIV. An ophthalmic referral at the time of presentation must be ensured by the treating physician. The ophthalmologist must take utmost care while examining and treating such patients to avoid patient to patient and patient to healthcare provider spread of HIV. A detailed ophthalmic examination for the various manifestations must be done and timely intervention for the same must be carried out which is critical to prevent ocular morbidity. Highly Active Anti Retroviral Therapy (HAART) is safe and has been instrumental in lowering sight threatening complications of HIV such as CMV retinitis.

Keywords: HIV; India; Ophthalmology; CMV Retinitis

HIV - India and the World

Human Immunodeficiency Virus (HIV) currently infects 35.3 million people across the world [1]. Overwhelming size of the Indian population makes it the country with the largest number of people living with HIV /AIDS (PLWHA). There are 2.09 million PLWHA in India and out of this number, approximately 145,000 are children [2]. Children (<15 yrs) account for 3.5% of all infections, while 83% are the in age group 15-49 years. Of all HIV infections, 39% (930,000) are among women [2].

With the advent of Antiretroviral Therapy (ART), the scenario is changing for the better. The number of people dying of AIDS-related causes fell to 1.8 million [1.6 million –1.9 million] in 2010, down from a peak of 2.2 million [2.1 million–2.5 million] in the mid-2000s [3]. A total of 2.5 million deaths have been averted in low- and middle-income countries since 1995 due to antiretroviral therapy being introduced, according to calculations by UNAIDS. [3] Much of that success has come in the past two years when rapid scale-up of access to treatment occurred; in 2010 alone, 700 000 AIDS related deaths were averted [3]. The proportion of women living with HIV has remained stable at 50% globally, although women are more affected in sub-Saharan Africa (59% of all people living with HIV) and the Caribbean (53%) [3].

There were 2.7 million [2.4 million–2.9 million] new HIV infections in 2010, including an estimated 390 000 [340 000–450 000] among children [3]. This was 15% less than in 2001, and 21% below the number of new infections at the peak of the epidemic in 1997 [3]. Thus we see that the number of people becoming infected with HIV is continuing to fall, in some countries more rapidly than others. HIV incidence has fallen in 33 countries, 22 of them in sub-Saharan Africa, the region most affected by the AIDS epidemic [3]. In India, the country with the largest number of people living with HIV, new HIV infections has fallen by 56% [3].

HIV and Eye

Ophthalmic manifestations of HIV infection are diverse. Both anterior and posterior segments of the eye can be involved and it may even lead to blindness [4]. The earliest studies on this subject stated the prevalence of ophthalmic manifestations of HIV infection ranging from 10 to 20% [4,5]. There is a lesser prevalence of ophthalmic manifestations of HIV infection in children as compared to adults as described in various studies [6-9]. Moreover the pattern of ophthalmic manifestations of HIV in paediatric patients has been found to be different from that found in adults [6-9]. Thus, it becomes challenging to screen carefully and thoroughly every HIV positive patient in order to pick up subtle, unconventional and unexpected manifestations.

Patients with visual disturbances or unmitting ophthalmic symptoms, regardless of CD4 cell count should be evaluated by an ophthalmologist. All areas of the visual system can potentially be affected in patients with HIV infection and thus a detailed ophthalmological examination is important [10] (Table 1).

Numerous ophthalmic manifestations of HIV infection may involve the anterior or posterior segment of the eye. Anterior segment findings include tumours of the periocular tissues such as Kaposis Sarcoma and a variety of infections such as uveitis, Herpes Zoster Ophthalmicus (Figure 1) and Molluscum contagiosus. Posterior segment changes include cytomegalovirus (CMV) retinopathy (Figure 2), outer retinal necrosis (Figure 3) and a number of opportunistic infections of the retina and choroid. (Table 2) The immune status of the patient is expected to influence the frequency and nature of manifestations in the eye. (Table 3) Partial immune system recovery following initiation of effective antiretroviral therapy may modify clinical presentation. In addition, in one eye, several infections may occur at the same time, rendering diagnosis and therapeutic intervention more difficult.

With the advent of drugs to control HIV infection, the incidence of complications has reduced but has not been eliminated [11]. For this reason, many individuals in training or recently in practice may have only a small experience with diseases such as CMV retinitis, progressive outer retinal necrosis, acute retinal necrosis, cryptococcal, syphilitic
and toxoplasmal infections (Figure 4). In addition, the many types of HIV related non-infectious retinopathy may make matters confusing or lead to misdiagnosis.

In India the first cases of HIV were diagnosed among sex workers in Chennai, Tamil Nadu by Simoes et al., in 1986 [12]. Biswas et al. reported the first two cases of ocular lesions in AIDS in India. The first case was a sub retinal yellow mass and the second case had CMV retinitis and cotton-wool spots [13]. Biswas et al. further did an elaborate study and documented the ocular disorders seen in the first 100 individuals known to be HIV-positive at a referral eye clinic in India between 1993 and 1998. Most of the patients (76%) in their study were in the 20-40 years age group. CMV retinitis (17%) and HIV retinopathy (15%) were the most common ophthalmic lesions in their study [14]. Another important study conducted at the apex eye institute in India in the post HAART era was by Gharai et al where 199 eyes of HIV positive patients were examined for ophthalmic manifestations. The median age of patients in their study was 34 years and 68% of the patients were on HAART. 45% patients in this study had ophthalmic manifestations, the most common being cytomegalovirus (CMV) retinitis (20%). Retinal detachment was seen in 70% (14/20) of CMV retinitis patients. HIV vasculopathy was seen in 11% (11/100) of patients. Other lesions observed in their study included immune recovery uveitis (IRU) (5%), acute retinal necrosis (ARN) (3%), choroiditis (2%), neuro-ophthalmic manifestations (12%), complicated cataract (6%), keratouveitis (1%) and corneal ulcer. Amongst those who had ophthalmic involvement in their study, about 50% patients had CD4 count below 100 cells/micro liter and 70% of the patients had CD4 count below 200 cells/micro liter [15].

Table 1: Various ophthalmological manifestations in HIV positive patients.

| Type                          | Manifestations                                                                 |
|-------------------------------|-------------------------------------------------------------------------------|
| 1 Allergic                    | Allergic conjunctivitis                                                       |
| 2 Autoimmune                  | Reiter’s syndrome, uveitis and vasculitis                                     |
| 3 Opportunistic infections    | Bacterial, mycobacterial, viral and fungal infection of the eye and adnexa   |
| 4 Neoplasia                   | Ocular Lymphoma                                                               |
| 5. HIV related                | HIV retinopathy, Cotton wool Spots                                           |
| 6. Neuro-ophthalmic           | Optic neuropathy, papilloedema, cranial nerve palsy, cortical blindness       |
| 7 Treatment/ drug related toxicities | Didanosine retinopathy, Rifabutin/ cidofovir related uveitis               |

Table 2: HIV and Retina.

| Disease                     | Fundus | Vitritis | Progression | CD4 cells/mm³ | Treatment                      |
|-----------------------------|--------|----------|-------------|---------------|--------------------------------|
| CMV                         | Diffuse/ unifocal/ multifocal retinitis with haem + granular border | Minimal | Slow | <100 | Systemic anti-CMV therapy, ART   |
| Toxoplasmosis               | Focal dense retinitis | Yes | Slow | <200 | As for cerebral toxoplasmosis |
| HIV micro-vasculopathy      | Multiple well defined cotton wool spots with small haemorrhages | No | Regresses | <250 | Nil |
| ARN                         | Widespread dense peripheral retinitis | Yes | Rapid early detachment | High dose acyclovir |
| PORN                        | Multifocal outer retinitis | No | Rapid early detachment | <50 | Combination antiviral |
| Syphilis                    | Papillitis, retinitis, choroiditis or uveitis | Yes | Any | As for neurosyphilis |
| Fungal retinitis (candida)  | Focal or multifocal vitritis, papillitis or retinitis | Yes | Any | Systemic and local antifungals |
| Intraocular lymphoma        | Diffuse or multifocal choroiditis | Yes | Slow | <50 | Radiotherapy plus chemotherapy |
| Cryptococcal choroiditis    | Multifocal discrete pale choroidal lesions | No | Slow | <200 | As for cryptococcal meningitis |
| Pneumocystis choroiditis    | Multifocal discrete pale flat choroidal lesions | No | Slow | <250 | Systemic PCP therapy |
| Histoplasmosis              | Multifocal choroiditis | No | Slow | Systemic antifungals |
| Tuberculous choroiditis     | Multifocal yellow/white choroiditis | Yes | | As for TB |

Figure 1: Herpes Zoster Ophthalmicus

Figure 2: CMV Retinitis.

Figure 3: Progressive Outer Retinal Necrosis.
Among Indian pediatric patients, Biswas et al. in their study reported that the spectrum of ocular lesions in children with HIV infection is different from that seen in adults. Vertical transmission was found to be the most common mode of infection (58.33%). Ocular lesions were found in 50% of patients, the most common ocular lesions being anterior uveitis and CMV retinitis (33% each) followed by retinal detachment (16.66%) and vitreous hemorrhage (16.66%) [16].

In the post HAART era, more elaborate studies need to be undertaken to compare our results from the pre HAART era which will enable us to know how the natural history of various manifestations have altered with increased survival of patients on ART. We also need to evaluate the newer challenges with ART. Some of these newer challenges being prolonged follow-up and close monitoring with increased lifespan of such patients on ART, regular follow up eye examinations, assessment of findings in relation to fluctuations in CD4 counts and monitoring of incidence of adverse ophthalmic side effects of ART.

In a country like India, other challenges which cannot be ignored are delayed presentation of patients to health care facilities, delayed diagnosis, increased frequency of malnutrition and susceptibility to infection which complicate disease presentation and the several social and economic factors which inhibit proper treatment compliance in our patients [17].

**Ophthalmic Practice and Spread of HIV**

HIV is present in very low quantities in tears and ocular tissues but the ophthalmologist is nonetheless cautious about any probable risk of transmission in the health care setting either from patient to patient or from patient to care provider [18]. Contact tonometry, Applanation tonometers, Perkins’ handheld applanation tonometer and Contact lens trial sets are possible modes of spread. Corneal transplantation is a possible route of viral transmission. HIV has been isolated from corneal cells and aqueous humour [19,20]. Donor corneas are often used within hours after enucleation, not allowing enough time for routine testing of the donor serum.

During clinical procedures the risk of getting HIV from seropositive patients is probably very small but it may be wise to wear a face mask when examining patients especially with pulmonary disease and HIV and if one is to perform procedures which involve more exposure to blood such as exenteration or dacryocystorhinostomy, universal precautions must be taken without fail.

**Conclusion**

Ophthalmic findings in HIV patients are manifold and some findings such as CMV Retinitis can even lead to blindness. Moreover, infections which are otherwise simple and inconsequential in a seronegative patient, can be tenacious in HIV positive patients. The challenges while treating HIV positive patients are immense and immune status of the patient plays a key role in determining outcomes. Early diagnosis, local and systemic methods of treatment such intravitreal Ganciclovir implants in cases of CMV retinitis have shown promising results in reducing ocular morbidities.

**References**

1. UNAIDS (2013) UNAIDS report on the global AIDS epidemic.
2. UNAIDS (2011) World AIDS Day Report 2011.
3. National AIDS Control Organization Annual Report 2012-13. Department of AIDS Control, Ministry of Health and Family Welfare.
4. Holland GN, Pepose JS, Petit TH, Gottlieb MS, Yee RD, et al. (1983) Acquired immune deficiency syndrome. Ocular manifestations. Ophthalmology 90: 859-873.
5. Freeman WR, Lerner CW, Mines JA, Lash RS, Nadel AJ, et al. (1984) A prospective study of the ophthalmologic findings in the acquired immune deficiency syndrome. Am J Ophthalmol 97: 133-142.
6. Denneyh PJ, Warman R, Flynnt JT, Scott GB, Mastrucci MT (1989) Ocular manifestations in pediatric patients with acquired immune deficiency syndrome. Arch Ophthalmol 107: 978-982.
7. Esposito S, Porta A, Bojaniin J, Guattieri L, Cesati L, et al. (2006) Effect of highly active antiretroviral therapy (HAART) on the natural history of ocular manifestations in HIV-infected children. Eye (Lond) 20: 595-597.
8. Ikoona E, Kalyesubula I, Kawuma M (2003) Ocular manifestations in paediatric HIV/AIDS patients in Mulago Hospital, Uganda. Afr Health Sci 3: 83-86.
9. Almeida FP, Paula JS, Martins MC, Sena DF, Cervi MC, et al. (2007) Ocular manifestations in pediatric patients with HIV infection in the post-HAART era in southern Brazil. Eye (Lond) 21: 1017-1018.
10. Lightman S (1991) HIV and Eye. (1st ed.) BMJ Books.
11. Holland GN (2008) AIDS and ophthalmology: the first quarter century. Am J Ophthalmol 145: 397-408.
12. Simees EA, Babu PG, John TJ, Nirmala S, Solomon S, et al. (1987) Evidence for HTLV-III infection in prostitutes in Tamil Nadu (India). Indian J Med Res 85: 335-338.
13. Biswas J, Madhavan HN, Badrinath SS (1995) Ocular lesions in AIDS: a report of first two cases in India. Indian J Ophthalmol 43: 69-72.
14. Biswas J, Madhavan HN, George AE, Kumarasamy N, Solomon S (2000) Ocular lesions associated with HIV infection in India: a series of 100 consecutive patients evaluated at a referral center. Am J Ophthalmol 129: 9-15.
15. Gharai S, Venkatesh P, Garg S, Sharma SK, Vohra R (2008) Ophthalmic manifestations of HIV infections in India: in HAART: analysis of 100 consecutive patients evaluated at a tertiary eye care center in India. Ophthalmic Epidemiol 15: 264-271.
16. Biswas J, Kumar AA, George AE, Madhavan HN, Kumarasamy N, et al. (2000) Ocular and systemic lesions in children with HIV. Indian J Pediatr 67: 721-724.
17. Mothi SN, Karpagam S, Swamy VH, Mamatha ML, Sarvode SM (2011) Paediatric HIV—trends & challenges. Indian J Med Res 134: 912-919.

18. Mueller AJ, Klauss V, Gürtler L, Geier S (1992) Infrequent detection of HIV-1 components in tears compared to blood of HIV-1-infected persons. Infection 20: 249-252.

19. Ablashi DV, Sturzenegger S, Hunter EA, Palestine AG, Fujikawa LS, et al. (1987) Presence of HTLV-III in tears and cells from the eyes of AIDS patients. J Exp Pathol 3: 693-703.

20. Kashiwagi K, Gohdo T, Sato S, Iijima H, Tsukahara S (2000) Detection of HIV-RNA in aqueous humor and subretinal fluid in an HIV carrier with rhegmatogenous retinal detachment. Jpn J Ophthalmol 44: 687-689.