

Ocular manifestations among HIV/AIDS patients; a case of Muhimbili National Hospital, Tanzania

Yusufali ME¹, Mafwiri MM¹, Sanyiwa AJ¹, Kisimbi SJ¹, Muhina C¹, Mosenene S¹, Sirili N²

¹Department of Ophthalmology, Muhimbili University of Health and Allied Sciences, Tanzania

²Department of Development studies, Muhimbili University of Health and Allied Sciences, Tanzania

Corresponding author: Dr. Milka M. Mafwiri, Department of Ophthalmology, Muhimbili University of Health and Allied Sciences, P.O. Box 65001, Dar-es-Salaam-Tanzania. Email: milkwisa@gmail.com

ABSTRACT

Objective: About 70-80% of HIV/AIDS patients develop an ocular complication at some point of their illness, at times causing blindness, ocular damage and even death. This study was conducted to determine the pattern of ocular manifestations of HIV/AIDS and their relationship to Highly-Active-Anti-Retroviral-Therapy and CD4+Tcells-count among HIV/AIDS patients at Muhimbili National Hospital.

Methods: Cross-sectional study among 296 systematically sampled HIV/AIDS patients. Data collection was by history taking, clinical examination, laboratory investigations and review of case notes. Analysis was aided by using SPSS version 17 software. Inferential statistics was performed and a $p < 0.05$ was considered significant.

Results: Of the 296 patients, 165(56%) were females. About 153(51.7%) patients were using Highly-Active-Anti-Retroviral-Therapy, 164(55.4%) and 66(20.3%) had CD4+Tcells-counts of >350 cells/ μ L and <200 cell/ mm^3 respectively. Ocular manifestations affected 124/296 (41.9%) patients. The prevalence of ocular manifestations was significantly higher among those not on Highly-Active-Anti-Retroviral-Therapy (67.1% vs 18.3%, $\chi^2=66.79$, $p < 0.01$) and among patients with CD4+Tcells-count <200 cells/ μ L (73.3% vs 29.9%, $\chi^2=34.1$, $p < 0.05$). The commonest manifestations among 592 eyes were optic atrophy 5.4(9.1%), cataract 25(4.2%), keratitis 23(3.8%), HIV-retinopathy 21(3.5%) and squamous cell carcinoma of the conjunctiva 16(2.7%).

Conclusion: Despite introduction of HAART, the prevalence of ocular manifestations in Dar-es-Salaam is still high. Further research on optic nerve disorders; awareness creation to inform patients, health personnel and the community; and to screen HIV patients for ocular manifestations are recommended.

Key words: CD4+Tcells, Cataract, HAART, HIV/AIDS, Optic atrophy, Ocular manifestations

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) has become one of the world's most serious health and development challenges. Currently approximately 34 million people are living with HIV infection and nearly 30 million people have died of AIDS-related causes¹. Majority (97%) of the cases reside in low- and middle-income countries, particularly in sub-Saharan Africa. In Tanzania the prevalence is 5.6% among adults. It is estimated that there are 1,400,000 people living with HIV^{2,3}.

Ocular manifestation/s is among the commonest sequel of HIV/AIDS and can be the first presenting sign of HIV infection⁴. In the eye the disease affects the adnexa, the anterior segment, the posterior segment, the orbit and neuro-ophthalmologic structures. About 70-80% of HIV/AIDS patients develop an ocular complication at some point of their illness⁵. Affected patients also may suffer from HIV related blindness whose prevalence range from 6.9-23%⁶.

Introduction of Highly Active Anti-Retroviral Therapy (HAART) has modified the clinical course of the disease leading to reduction in the prevalence of HIV/

AIDS related complications⁷. In sub-Saharan Africa the prevalence of ocular manifestations vary depending on the setting. Studies conducted before introduction of HAART showed higher prevalence than those conducted after introduction of HAART. Among the reported prevalence in Africa are: 12.3% in Nigeria⁸, 33.3% in Mali⁹ and 21.4% in Gondar- Ethiopia¹⁰, 77% in Kenya¹¹ and 76% in Tanzania¹².

Lower CD4+Tcells counts are associated with higher prevalence and blindness due to ocular manifestations⁴. Anterior segment ocular manifestations have been found to be associated with higher CD4+Tcells count compared to posterior segment ones which seem to be associated with the lowest counts^{5,13}. Studies done in Africa showed a prevalence of ocular manifestations of between 32.8%-91.7% in patients with CD4+Tcell counts of <200 cells/ μ L⁴.

Highly Reactive Anti-Retroviral Therapy was introduced at Muhimbili National Hospital in November 2004. The current criteria for initiation of HAART to a patient are (1). A CD4+Tcell count of <350 cell/ μ L, and (2) HIV clinical stage 3 and 4. Since then, no studies have been conducted to document the prevalence and types of HIV ocular manifestations in Tanzania and their

relationship with HAART and CD4+Tcells count. It is also not known whether HIV patients are aware of the effects of HIV on their eyes. The study was conducted to describe the pattern of ocular manifestations and their relationship to HAART use and CD4+Tcell counts among HIV/AIDS patients attending the HIV clinic at Muhimbili National Hospital for planning purposes.

MATERIALS AND METHODS

Design: This was a hospital based cross-sectional study conducted for a period of one year from April 2013 to April, 2014.

Setting: This study was conducted at Muhimbili National Hospital (MNH). Data collection was carried out at the HIV clinic; this clinic provides HAART and counselling services to about 100 newly diagnosed and follow-up patients daily from Monday to Friday.

Study population: All adult patients aged 18 years and above who were attending the HIV clinic at MNH for treatment and care were eligible for the study. This age group was selected as it is possible to assess awareness and visual acuity compared to children. They are also the main attendees of the clinic.

Sampling and sample size: Patients were selected using systematic sampling and the estimated sample size to give a precision of 0.05% at a confidence interval of 95% was 290 patients.

Data collection: Patients were selected at the HIV clinic and sent to the eye clinic. Systemic sampling was employed where every 5th patient on the list of 100 patients listed to attend the clinic on the particular day was selected, informed about the study and requested to participate. Those who consented to participate were initially interviewed on awareness about effects of HIV on the eye. Records were reviewed for demographic characteristics and CD 4+Tcell count taken within six months. Ocular examination included best corrected

visual acuity test, intraocular pressure measurements, examination of the adnexa, extra ocular motility, alignment, dilated fundoscopy and cranial nerve function tests. Study instruments included the Snellen literate and illiterate E charts, non-contact tonometer, direct ophthalmoscope, 20 D Volk lens, 90 D Volk lens the Goldman 3 mirror lens, slit lamp biomicroscope and fluorescein dye strips. Brain computerized tomography (CT-Scan), Magnetic resonance imaging (MRI) and blood toxoplasma antibody depending on the need were performed. Eye lid and conjunctival tumours were confirmed by histopathology.

Data analysis: Data were analyzed using SPSS version 17 software. Descriptive statistics were used to summarize and describe the data. The relationship between independent variables and HAART and CD4+Tcell counts was analysed using Chi squared test and a $p < 0.05$ considered to ascertain whether there was a significant difference between variables.

Ethical issues: This study was ethically approved by the Ethics and Research Committee of Muhimbili University of Health and Allied Sciences (MUHAS). Permission to conduct the study was sought from the relevant hospital authorities. Written informed consent was obtained from each participant. Confidentiality and privacy was maintained throughout the study. Data was stored safely and used for the purposes of the study only.

RESULTS

Two hundred and ninety six patients were recruited for the study and all were included in the analysis. The mean age of study participants was $38.6(\pm 0.7)$ and the age range was 21-70 years. Majority (216, 73%) of participants were aged between 31-50 years. About 165 (56%), of participants were females. More than 50% of the participants were on HAART. A few of them were aware of ocular manifestations (39.5%).

Table 1: The distribution of the study population by demographic features and HAART use

Demographic feature		On HAART			P-value
	Frequency	Yes No. (%)	No No. (%)	Total No. (%)	
Age (years)	<30	10 (62.5)	6 (37.5)	16 (62.5)	0.402
	31 – 40	54 (49.1)	56 (50.9)	110(37.2)	
	41 – 50	61 (57.5)	45 (42.5)	106(35.8)	
	51 – 60	20 (45.5)	24 (54.5)	44(14.9)	
	>60	8 (40)	12 (60)	20(6.7)	
Total		153(51.7)	143(48.3)	296(100)	
Sex	Male	69 (52.7)	62 (47.3)	131(44.3)	0.663
	Female	84 (50.9)	81 (49.1)	165(55.7)	
Total		153(51.7)	143(48.3)	296(100)	

Table 2: The distribution of ocular manifestations by HAART use among the study population

Ocular manifestations	HAART use		Total No. (%)
	Yes No. (%)	No No. (%)	
Yes	28 (18.3)	96 (67.1)	124 (41.9)
No	125 (81.7)	47 (32.9)	172 (58.1)
Total	153 (100)	143 (100)	296 (100)

Out of 296 participants, 124 (41.9%) had ocular manifestations and 70 (56.5%) of them had bilateral involvement. Twenty four (8.1%) patients had more than one condition. Slightly more females (71/165, 43.0%) than males (53/131, 40.4%) were affected by ocular manifestations. Two thirds (85/124, 68%) of patients with ocular manifestations were in the age group between 31-50 years. Ninety six (67.1%) eyes were of patients in the group not on HAART compared to 28/153 (18.3%) affected eyes among those on HAART. Being affected with ocular manifestations of HIV was associated with not using HAART ($p<0.01$)(Table 2) but not associated with age ($p=0.5$) or gender ($p=0.09$).

Table 3: The prevalence of ocular manifestation by CD4+Tcells count among the study population (n=296)

Level of CD4 count (cells/ μ L)	Ocular manifestation		Total No. (%)
	Yes No. (%)	No No. (%)	
<200	44 (73.3)	16 (26.7)	60 (100)
200 – 350	31 (43.1)	41 (56.9)	72 (100)
>350	49 (29.9)	115 (70.1)	164 (100)
Total	124(41.9)	172(58.1)	296 (100)

$X^2=34.13$, $p<0.044$

More than half (164/296, 55.4%) of the study population had CD4+Tcells count above 350 cells/ μ L while 60/296 (20.3%) had lowest CD4+Tcells counts <200 cell/ μ L. Patients with the lowest CD4+Tcells count of <200 cells/ μ L had the highest (44/60, 73.3%) prevalence of ocular manifestations. The association between having ocular manifestation and CD4+Tcells count was statistically significant. ($p<0.05$) (Table 4).

A total of 194(32.7%) eyes were affected by various HIV ocular manifestations. The leading subtypes were neuro-ophthalmologic (79/592, 13.3%), anterior segment

74/592(12.5%), posterior segment (31/592, 5.2%) and adnexal (10/592, 1.6%) affected eyes.

Table 4: Ocular manifestation sub-type among 194 affected eyes and HAART use

Ocular manifestation type	HAART use			P-value
	Yes No. (%)	No No. (%)	Total No. (%)	
Adnexal (n=10)	1(10)	9(90)	10(100)	0.69
Anterior segment (n=74)	25(33.8)	49(66.2)	74(100)	0.01
Posterior segment (n=31)	2(6.4)	29 (93.5)	31(100)	0.54
Neuro- ophthalmic (n=79)	19 (24.1)	60 (75.9)	79(100)	0.04
Total	47(24.2)	147(75.8)	194(100)	

Not using HAART was significantly associated with a higher prevalence of neuro-ophthalmic ($p=0.04$) and anterior segment manifestations ($p=0.01$) respectively (Table 4).

Neuro-ophthalmic ocular manifestations were significantly associated with higher CD4+Tcell counts ($p=0.04$) while adnexal, anterior and posterior segment manifestations were not. Optic atrophy was the commonest manifestation which affected 54/592(9.1%) eyes and was the leading neuro-ophthalmological lesion (54/79, 68%). Other common lesions were cataract (25/592,-4.2%), keratitis (23/592, 3.8%) and HIV retinopathy (21/592, 3.5%) (Table5). There was only one eye affected by CMV retinitis. A third (31/79, 39.2%) eyes with optic atrophy were of patients with higher CD4+ T cell counts of >350 cell/ μ L while only 9/79 (16.7%) eyes were of patients with the lowest CD4 T-cell counts of <200 cells/ μ L.

Table 5: The relationship between sub-type and diagnosis of ocular manifestations and CD4+T cell counts (n=194 eyes)

Ocular manifestation type	Diagnosis	CD4 counts level (cells/ μ L)			
		<200	200-350	>350	Total
		No. (%)	No. (%)	No. (%)	No. (%)
Adnexal	Herpes zoster ophthalmicus	5(83.3)	1(16.7)	0(0)	6(100)
	Kaposi's sarcoma	2(1010)	0(0)	0 (0)	2(100)
	Molluscum contagiosum	0(0)	1(50)	1 (50)	2(100)
	Total	7(70)	2(20)	1(10)	10(100)
Anterior segment	Keratoconjunctivitis sicca	2(100)	0 (0)	0(0)	2(100)
	Conjunctiva growths	8(50)	6(37.5)	2 (12.5)	16(100)
	Keratitis	6(26.1)	10(43.5)	7 (30.4)	23(100)
	Iridocyclitis	4(50)	3(37.5)	1 (12.5)	8(100)
Posterior segment	Cataract	5(20)	8(32)	12(48)	25(100)
	Total	25(100)	27(100)	22(100)	74(100)
	HIV retinopathy	16(76.2)	1(4.8)	4 (19)	21(100)
	CMV retinitis	1 (100)	0 (0)	0 (0)	1(100)
Neuro-ophthalmological	Chorioretinitis	0 (0)	0 (0)	2 (100)	2(100)
	Toxoplasma retinochoroiditis	1 (14.3)	1 (14.3)	5 (71.4)	7(100)
	Total	18(58.1)	2 (6.5)	11 (35.5)	31(100)
	Optic atrophy	9 (16.7)	19(35.2)	26 (48.1)	54(100)
Neuro-ophthalmological	Papilloedema	6 (46.2)	4 (30.8)	3(23.)	13(100)
	Papillitis	5 (41.7)	5 (41.7)	2 (16.7)	12(100)
	Total	20 (25.3)	28(35.4)	31(39.2)	79(100)
					P=0.04

DISCUSSION

This study aimed at describing the pattern of ocular manifestations and their relationship to HAART use and CD4+Tcell counts among HIV/AIDS patients attending the HIV clinic at Muhimbili National Hospital for planning purposes. Results show that the study population age range was 21 years to 73 years with a mean age of 38.65 (± 0.74) years similar to the findings by Azonobi *et al*¹³ and Bekele *et al*¹⁴ in Ethiopia. The similarity in the most affected age group is a reflection the age distribution of HIV prevalence in Africa where young sexually active adults are commonly affected.

The lack of awareness about the effects of HIV on the eye among 60% of the study population signifies inadequate exposure to appropriate health education on HIV complications. Lack of awareness leads to delay

in seeking appropriate care, late diagnosis, poor post-treatment outcome, visual loss and loss of the eye in case of advanced carcinoma of the conjunctiva.

The overall prevalence of ocular manifestations in this study was 124(41.9%) which is lower than studies done during the pre-HAART era in Tanzania 76%¹² and other countries in sub-Saharan Africa^{10,11,16}. The prevalence is however higher than that reported from similar tertiary centres providing HAART services in Ethiopia 25.3%¹⁴, South India 24.32%¹⁷ and Korea (28.5%)¹⁸. The use of HAART is known to modify the clinical presentation of HIV such that the occurrence of complications and opportunistic infections are reduced. The high prevalence despite HAART in this study is probably related to the fact that about half of the study population were not on HAART. Patients were not on HAART either because they did not meet the criteria

for starting HAART or they presented late and were still in the process of being investigated and a decision on their treatment had not been reached. In this group, the natural history of HIV progressed unchecked leading to development of complications. Indeed the prevalence of ocular manifestations among patients not on HAART was three times higher than those on HAART. Similar to studies in other Asian and African countries^{10,16-18}, the prevalence of ocular manifestations in this study was significantly higher among patients with lowest CD4+Tcells.

The finding that neuro-ophthalmic manifestations were the commonest followed by anterior segment is in agreement with a study in Ethiopia¹⁰. Neuro-ophthalmic manifestations are not a marker of disease severity and could therefore occur at any stage of the disease¹⁹.

In this study, neuro-ophthalmic manifestations were significantly related ($p < 0.05$) to not using HAART and a lower CD4+Tcell counts. The fact that optic atrophy was the commonest lesions is worth noting because the condition causes permanent visual loss. Half (48%) of the lesions occurred in patients with higher CD4+Tcell counts of $> 350/\mu\text{L}$. This group of patients could either be on treatment with immune recovery and /or not yet started on treatment as they had not met the criteria for starting HAART. In HIV/AIDS the optic nerve may be damaged through various mechanisms including infection, inflammation infiltration, ischemia, increased intracranial pressure and compression. The condition can also develop in the absence of known prior history of optic nerve disease²⁰. In the present study, it was not possible to ascertain the causes of optic atrophy or other neuro-ophthalmic conditions like papillitis and papilledema due to limited diagnostic capacity. Because optic atrophy and other neuro-ophthalmic disorders have a potential to cause blindness it is important to screen all patients living with HIV for optic nerve disorders in order to initiate treatment even when the CD4+T cells count level is higher than $350/\mu\text{L}$. Early initiation of HAART has been shown to improve visual prognosis of optic nerve disorders²⁰.

Patients with HIV have a higher prevalence of cataracts²¹ than the general population and such cataracts correlate with lower CD4+Tcells count²². In this study cataracts were among the commonest anterior segment manifestations. Screening for ocular manifestation among HIV patients can identify those who need cataract surgery.

In this study we used CD4+Tcell counts tested within 6 months that may have increased or decreased by the time data was collected thereby giving wrong estimations of patients with lower or higher CD4+Tcell counts. Additionally, the study did not explore the reasons for not being on HAART for patients who met the criteria by having CD4+Tcell counts of $< 350 \text{ cells}/\mu\text{L}$. Such information would help in establishing strategies to improve care at the HIV clinic. Being a hospital based study at a referral hospital in Tanzania, a highly selected group of patients was studied hence results from this study may not reflect the situation in the community.

CONCLUSIONS

The prevalence of ocular manifestations among patients attending the HIV clinic at Muhimbili National Hospital is high. Most lesions occurred in patients who were not on HAART and whose CD4+Tcells counts was $< 200 \text{ cells}/\mu\text{L}$. Neuro-ophthalmic manifestations were the commonest. Optic atrophy, cataract, keratitis, HIV retinopathy and squamous cell carcinoma of the conjunctiva were the main diagnoses.

RECOMMENDATIONS

It is recommended that routine ocular screening of all patients with HIV be established to identify patients with ocular manifestations, ensure early diagnosis and appropriate treatment of the ocular condition and start HAART as per treatment guidelines. Patients with lower CD4+Tcell counts should be prioritized for screening where eye personnel are inadequate. Creation of awareness to both patients and health personnel on importance of early health seeking behaviour and referral for ocular examination of patients with HIV should be emphasized. Further studies are required to establish the causes of optic atrophy in this population are required.

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The authors have no proprietary interest in any materials mentioned in this article.

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