Ocular manifestations of HIV/AIDS at Moi Teaching and Referral Hospital (AMPATH Clinic)

AUTHORS

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ABSTRACT

Objective: **To determine the prevalence and pattern of ocular conditions in HIV/AIDS patients attending HIV/AIDS care clinic (AMPATH).**

Design: **Hospital-based cross sectional study.**

Setting: **Moi Teaching and Referral Hospital (AMPATH CLINIC) ,Eldoret, Kenya.**

Subjects: **HIV/AIDS patients seen at AMPATH, clinic.**

Results: **Two hundred patients with HIV/AIDS were examined. The overall prevalence of ocular findings was 154 patients (77%). One hundred and eighteen patients (59%) were on ARV therapy. The main findings were posterior segment lesions (53%), anterior segment disorders (26.5%). Posterior segment findings included; Retinal microvasculopathy (75 patients ,37.5%), chorioretinitis (9 patients ,4.5%), vitreous opacities (8 patients, 4%), macula edema (8 patients, 4%) and CMV retinitis (5 patients ,2.5%). Fibrous membrane attached to the iris mostly near the pupillary margin (37 patients, 18.5%) and iridocyclitis (11 patients, 5.5%) were the main anterior segment findings. Conjunctival growths (13 patients, 6,5%) and Kaposi (10 patients, 5%), conjunctival microvasculopathy (8 patients, 4%) and molluscum contagiosum (5 patients, 2.5%) were the main ocular adnexal findings. Tuberculosis was the main systemic findings (53%). This study found that ocular findings are directly related to the severity of clinical disease staging (e.g. WHO stages III and IV) and severity of immune suppression (CD4+ count).**

Conclusion: **The results of this study suggest a high prevalence of ocular findings in adolescents and adults with HIV/AIDS. Retinal microvasculopathy was the commonest posterior segment finding observed. Further studies are needed to investigate the unusual findings of the fibrous membrane attached to the iris observed in this study.**

INTRODUCTION

Practicing ophthalmologists are faced with the challenges to recognize and treat potentially sight threatening conditions and to identify unusual presentations.

The Human Immuno-deficiency Virus (HIV) infection has spread worldwide with various adverse health economic implications particularly in the developing world. New data show global HIV prevalence, the percentage of people living with HIV has leveled off and that the number of new infections has fallen, in part as a result of the impact of HIV programmes(1). However in 2007 33.2 million (30.6 – 36.1 million) people were estimated to be living with HIV, 2.5 million (1.8 – 4.1 million) people became newly infected and 2.1 million (1.9 – 2.4 million) people died of AIDS.

There were an estimated 1.7 million (1.4 -2.4 million) new HIV infections in sub-Saharan Africa in 2007, a significant reduction since 2001. However the region remains most severely affected. An estimated 22.5 million (20.9 -24.2 million) people living with HIV or 68% of the global total, are in sub-Saharan Africa(1).

It is reported in literature that among the individuals infected with HIV; approximately 70-80% will be treated for an HIV associated eye disorder during the course of the illness. In general CD4 plus lymphocyte count has been used to predict the onset of certain ocular manifestations in patients who are HIV positive; CD4 count less than 100 cells/mm^3 is associated with retinal or conjunctival microvasculopathy, CMV retinitis, mycobacterium avium complex

infection, cryptoccosis, microsporidiosis, HIV encephalopathy, progressive multifocal leukoencephalopathy

METHODS

A hospital – based cross sectional study was conducted. HIV/AIDS patients aged 15 years old and above attending the AMPATH Clinic at Moi Teaching and Referral Hospital (MTRH) were recruited daily into the study. The overriding goal of AMPATH is to establish a working model of both urban and rural comprehensive HIV preventive and treatment services, representing the unique attributes of academic institutions. AMPATH has structured its patients care programmes to simultaneously provide HIV related teaching and research. The pilot phase of AMPATH began in November 2001.

The study was conducted between 31st March and 21st April 2008. The minimum sample size was calculated to be 200 and all consecutive patients fulfilling the inclusion criteria were included. Patients were randomly recruited daily from the AMPATH clinic. On average, about 100 patients were seen every day. Daily, only 20 patients were randomly selected for the study.

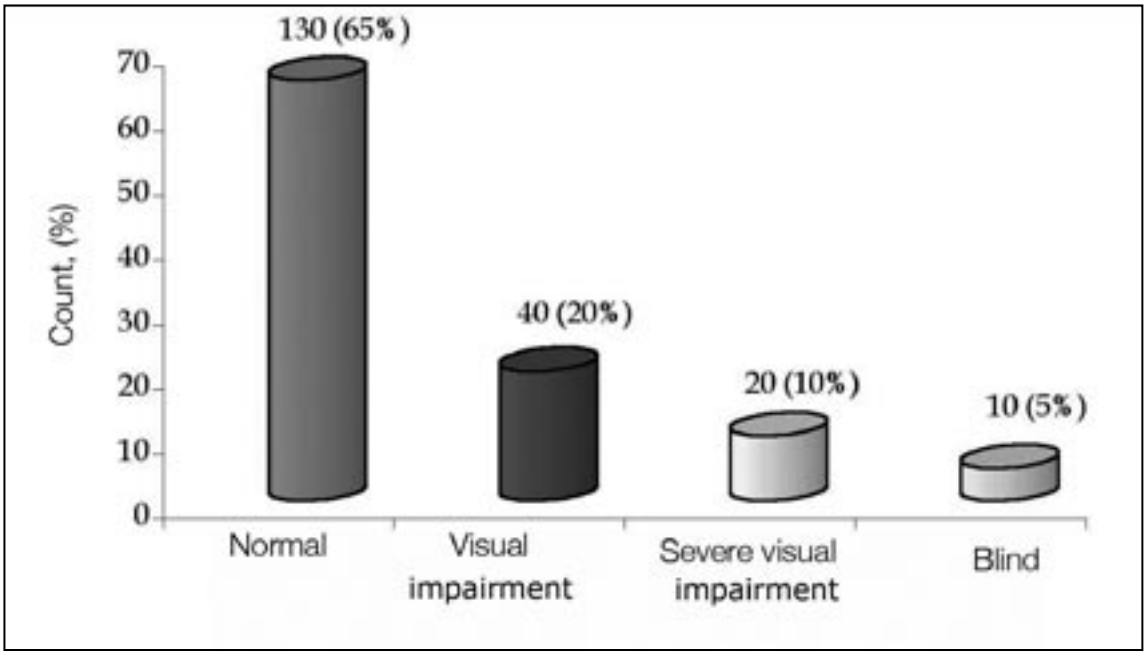
Upon arrival at the clinic, patients were allocated numbers from 1 to 100. The first patient (number 1) was picked, followed by every other 5th patient (i.e. patients number 5,10,15, etc..).

The aims and the procedures of the study were explained and those who consented to participate were examined in the Eye Clinic. In the clinic visual acuity was assessed using Snellen chart. Adnexal and anterior segment were assessed using slit –lamp. Dilated fundus examination was done using a direct or binocular indirect ophthalmoscope and slit lamp biomicroscopy with a + 90 D loupe where appropriate. Ethical approval was obtained from the Moi Teaching and Referral Hospital Institutional Research and Ethics Committee (IREC).

RESULTS

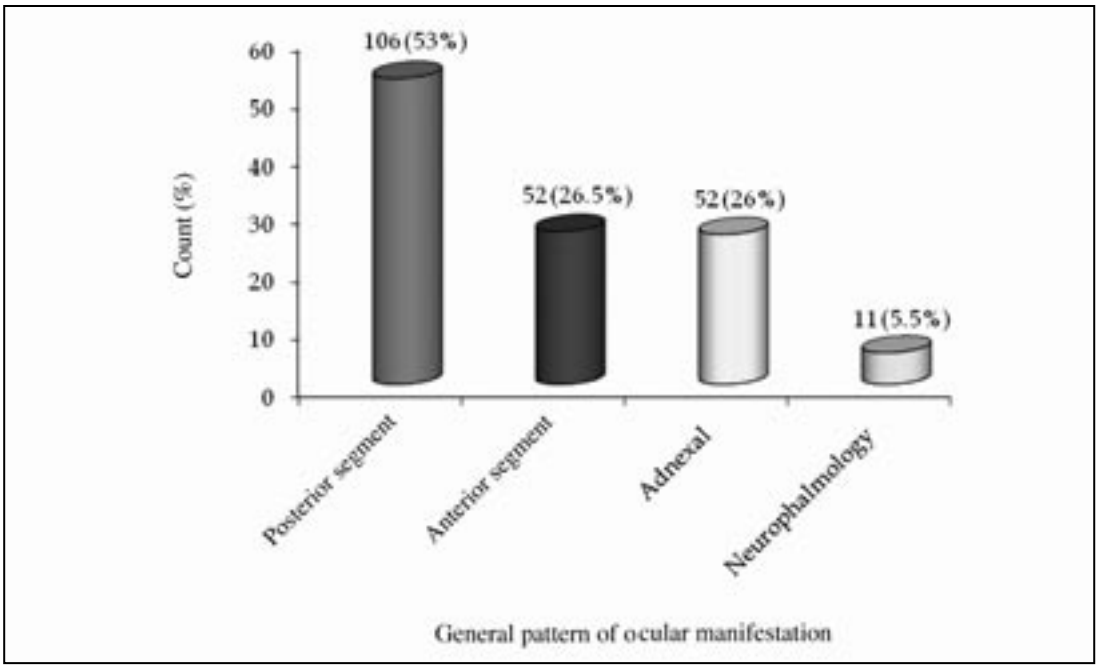
A total of 200 HIV/AIDS patients were recruited in the study. The age ranged from 15 years to 70 years with a median of 36 years and the interquantile range was 32 – 44 years. There were 132 females (66%) and 68 males (34%). From the report for past and current history on systemic ailments, this study reported pulmonary tuberculosis in 43 patients (22.5%) and oropharyngeal candidiasis in 19 patients (9.5%). One hundred and eighteen patients (59%) were on ARV therapy and 154 patients (77%) had ocular findings. The ophthalmic examination revealed posterior segment findings in 53% followed by anterior segment (26%) and adnexal findings (26%). Retinal microvasculopathy (75 patients) were the main posterior segment finding and iris/pupil fibro membrane were the main anterior segment finding

Figure 1: WHO visual acuity classification in better eye (n = 200)



Five percent of the study participants were blind in this study based on the WHO ICD – 10 classifications. All the five patients with CMV retinitis had bilateral involvement and all of them were in WHO category of blindness. Also in this group were patients with bilateral optic atrophy and some with bilateral chorioretinitis. Severe visual impairment and visual impairment were mostly due to a combination of anterior and posterior segment features.

Figure 2: Pattern of ocular manifestation (n = 200)



Most ocular manifestations were noted in the posterior segment (53%). In the anterior segment, iridocyclitis was predominat in patients with posterior segment findings such as retinal microangiopathy and chorioretinitis.

Figure 3: Posterior segment findings (n = 103)

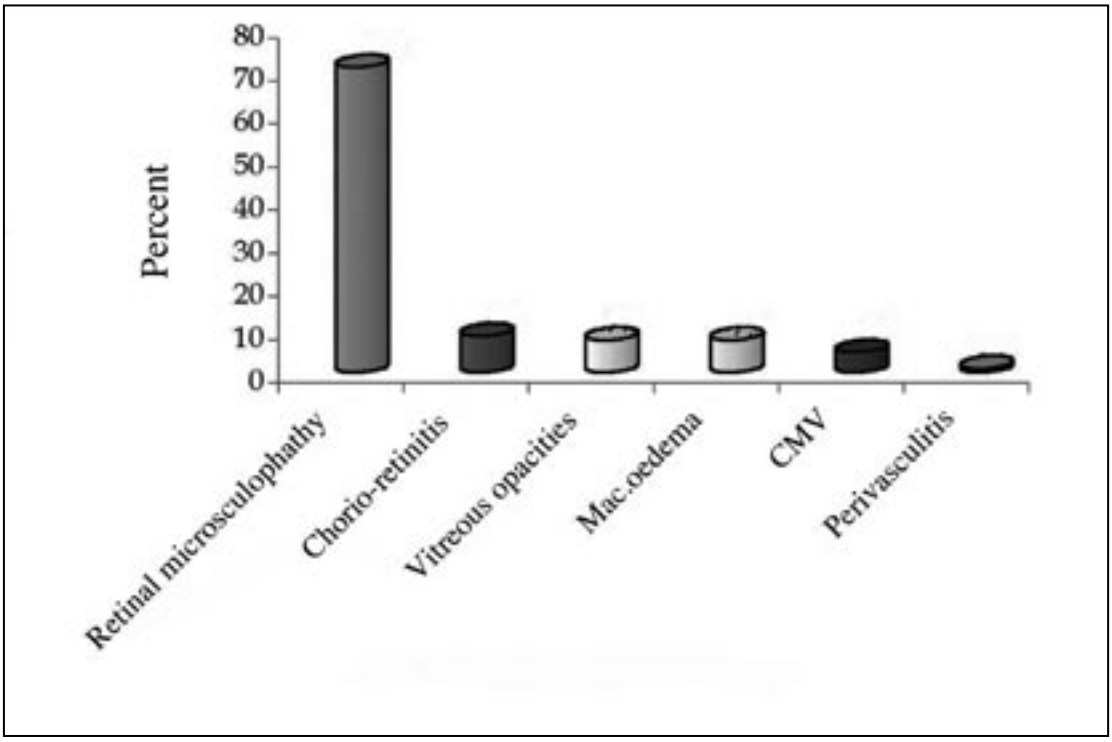
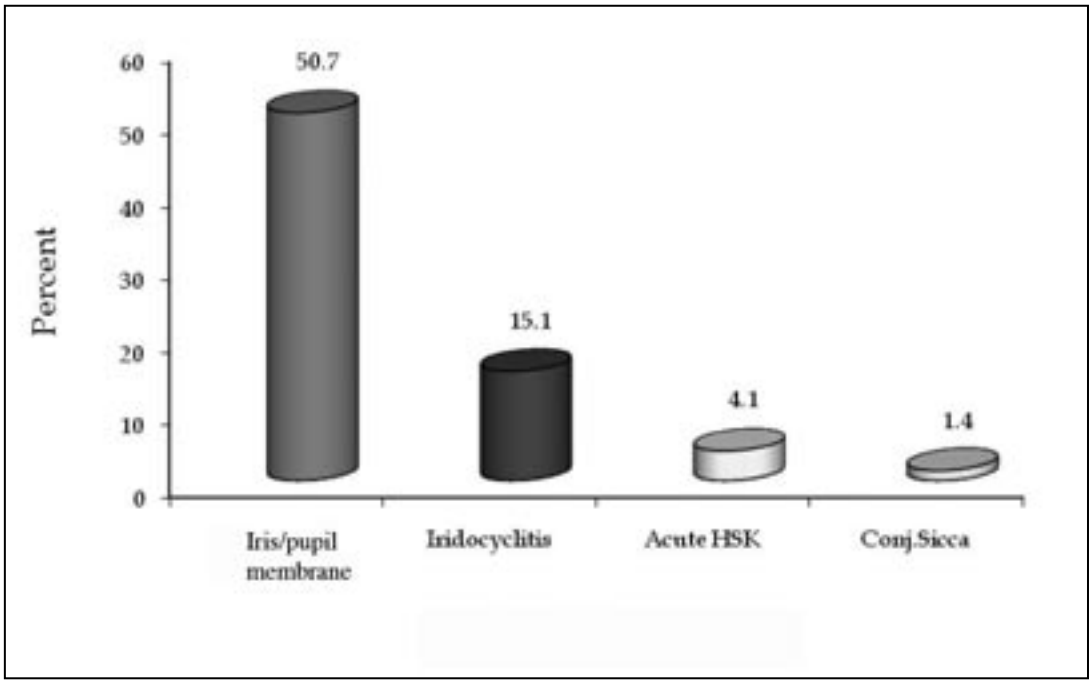
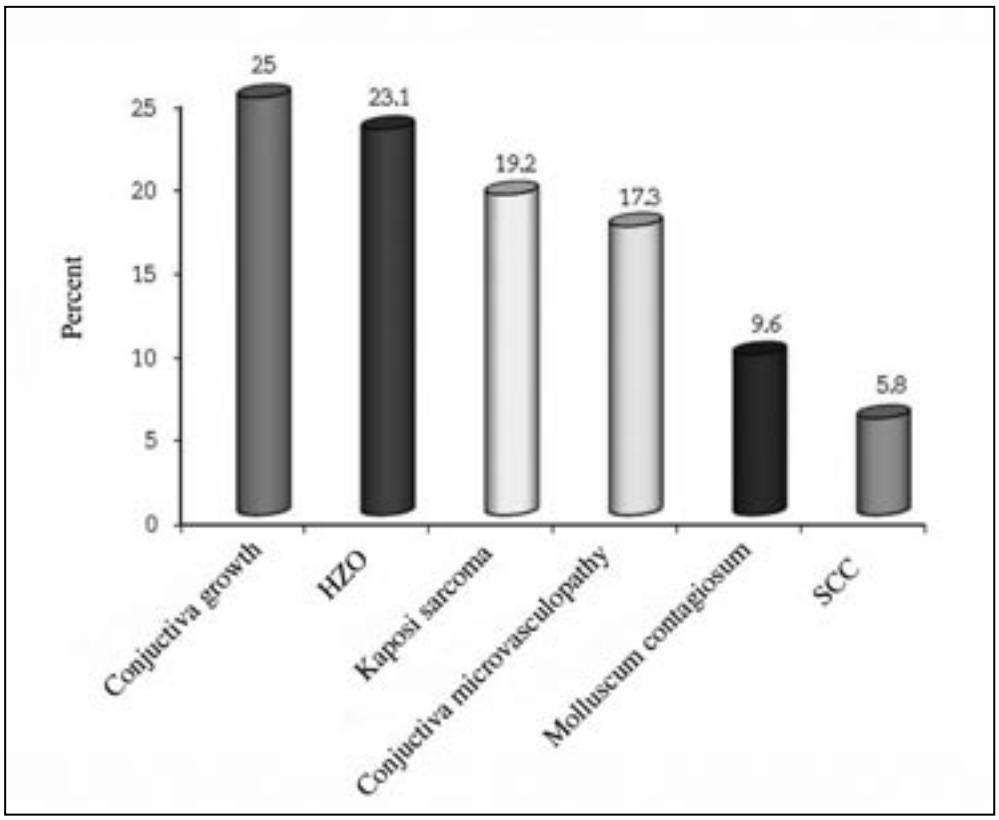


Figure 4: Anterior segment findings (n = 52)



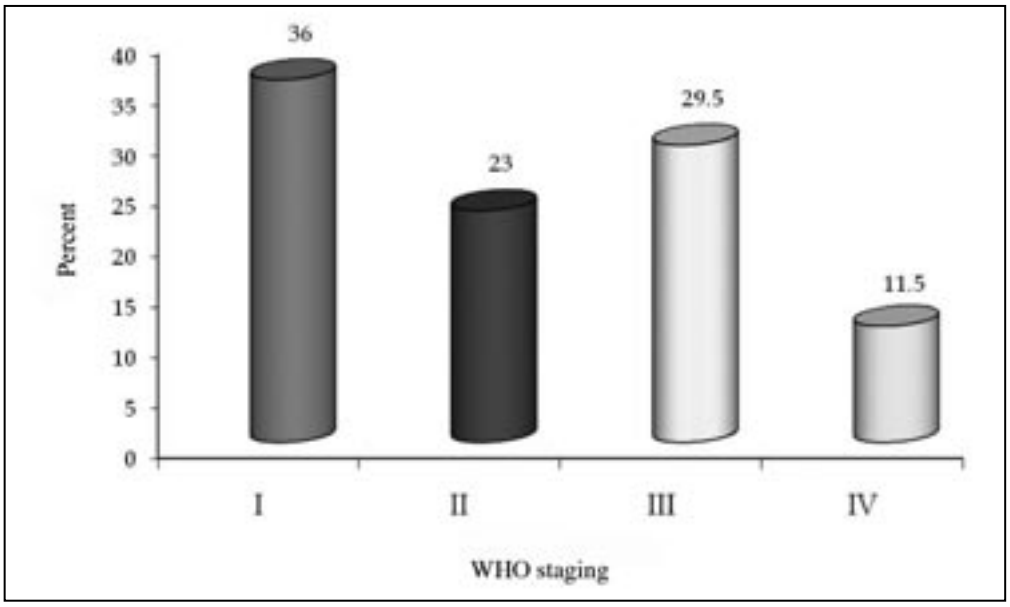
Cyclitic pupillary membranes were the commonest anterior segment finding (50.7%). The diagnosis of acute simplex keratitis was based on the clinical picture. The conjunctival growths noted were suspicious lesions. They were not degenerations like pingueculas. Squamous cell carcinoma (SCC) confirmed by histology was noted in 5.8% of the patients.

Figure 5: Adnexal findings (n = 52)



HZO = Herpes Zoster Ophthalmucis
SCC = Squamous Cell Carcinoma

Figure 6: HIV/AIDs staging (WHO classification; n = 200)



Forty one percent of the participants were in stage III and IV as graded by the AMPATH physicians. By definition, these are patients all eligible for HAART by WHO recommendations.

Table 1: Association between ocular manifestation and current CD4-count (n = 200)

CD4-Count	(n)	Ocular manifestation, n (%)	OR 95%CI	P-value
0 – 100	22	21 (95.5)	5.7 (0.77 – 117.30)	0.044
101 – 200	32	31 (96.9)	9.1 (1.26 – 184.14)	0.021
201 – 300	30	26 (86.7)	1.7 (0.51 – 6.12)	0.500
301 – 400	33	38 (75.7)	0.9 (0.33 – 2.45)	0.975
401 – 500	37	28 (75.7)	0.7 (0.28 – 1.79)	0.975
500 +	46	29 (63.0)	0.28 (0.13 – 0.64)	0.001

There was a significant association between current CD4 count of between 0 – 100, 101 – 200 and 500+ and ocular manifestations with a p-value of less than 0.05. Participants with CD4 counts of between 0 – 100 were 5.7 times more likely to have ocular manifestations than participants with CD4 counts of >100.

Table 2: Association between ocular manifestation WHO staging and ARV treatment (n = 200)

On ARV	(n)	Ocular manifestation, n (%)	OR 95%CI	P-value
Yes	(118)	106 (68.8)	6.3 (3.0 – 13.1)	*<0.001*
WHO Stage				
I	(72)	48 (66.7)		
II	(46)	37 (80.4)	-	*<0.001*
III	(59)	54 (91.5)		
IV	(23)	22 (95.7)		

There was a significant association between ocular manifestation, patients on ARV and WHO staging with p< 0.001. Patients who were on ARV were 6.3 times likely to have ocular manifestations.

Table 3: Factors associated with presence of ocular manifestations (n = 200)

Factor	Parameter estimates	Std. error	P-value
Age	0.068	0.024	*0.004*
AZT use	-2.99	1.36	*0.028*
On ARV	-4		

On logistic regression, only age (p=0.004), AZT (p=0.028) and ARV usage (p=0.029) were significant.

DISCUSSION

In this series at AMPATH clinic in Western Kenya, a total of 200 HIV/AIDS patients were recruited and examined. All participants were out patients in fair general condition. They were on follow up and on management for management for HIV/AIDS in the AMPATH clinic. More than 70% of the patients fell in the 25-44 years age group considered the high risk group for HIV infection. The age distribution could be explained by the mode of spread of HIV in Kenya. Heterosexual infection is the commonest mode and this age group is the most sexually active. Female to male ratio was 2:1, females constituting 66%. In the AMPATH clinic register females account for about 65% of the patients. This finding could be due to the slightly higher prevalence of HIV in females than males. Females also accept their status more easily than males hence they seek health care more often as noted by Nascop (2).

Visual acuity was normal in 65% of the patients, 20% had visual impairment and 5% were blind by WHO standards (Figure 1). The significant causes of blindness were bilateral fulminant CMV retinitis involving the macula and optic nerve atrophy. In Ethiopia, Giorgis *et al* also noted that the leading cause of blindness was CMV retinitis. They also noted Herpes Zoster Ophthalmicus (HZO) as significant cause of unilateral blindness (3).

It was noted that 77% of the patients had some form of ocular manifestations. These findings are close to the results noted in Cameroon (63.2%) by Mvogo *et al* (4). In Dakar, Senegal Ndoye *et al* found a prevalence of 52.3% (5). In Ethiopia, Giorgis *et al* found ocular manifestations in 32.8% (3). The higher prevalence noted in this study is probably due to the fact that 93% of the patients were on ARVs which is high as compared to the studies above. Mvogo *et al* (4) actually pointed out that with improvement of access to antiretroviral therapy; the ocular manifestations of HIV/AIDS become more common. ARVs are also indicative of severe disease on initiation of the systemic therapy in patients with low CD counts.

In a review article by Al- Fat *et al* they noted that ocular manifestations may occur in about 75% of HIV/AIDS patients in the course of their disease (6) and suggested that with improvement of treatment and patients survival, ophthalmic complications are now being seen with increasing frequency in AIDS, occurring in up to 75% of patients during the course of the disease.

Ocular findings in this study were more common in the posterior segment (53%), followed by the anterior segment (26.5%). Adnexal manifestations were noted in 26.5% of the patients and neuro ophthalmic manifestations in 11%. This is consistent with Jabs *et al* observations in the USA who also noted that intraocular inflammation and other posterior segment manifestations is becoming a predominant feature with the exception of CMV retinitis (7).

This study found CMV retinitis in 2.5% of the cases. Findings in other studies range from <1% to 20%. Asseffa *et al* (8), in Ethiopia and Jabs *et al* (7) in the USA found in 14%. In Ethiopia, Giorgis *et al* (3) in a study in the armed forces found uveitis and CMV retinitis in 4 out of 65 patients (6.2% each). In Gambia Jaffar *et al* (9) found no cases of CMV retinitis but cotton wool spots were noted and their conclusion was that CMV retinitis is less common in Gambia, than in developed countries. These varied findings in the prevalence of CMV retinitis could be explained by the study design, the sample size

and the effects of ART on the CMV virus. There is a substantial decline in the incidence of CMV retinitis from the pre-HAART era (7).

Retinal microvasculopathy was the most common posterior segment finding seen in 37.5% of the patients. Only 2.5% of the patients had presumed CMV retinitis with poor vision and 4.5% had other forms of chorioretinitis apparently not related to CMV. Some of chorioretinal lesions may have been ocular TB as they occurred all in patients on TB treatment. However there were no classical choroidal granulomas . CMV retinitis was noted only in patients with a CD4 count of less than 100 while the HIV microangiopathy was also noted in CD4 counts of greater than 500. Nwosu *et al* at the Guinness Eye Centre in Nigeria found bilateral CMV retinitis in 6% of the patients. The CD4 count was less than 100 in all CMV patients as observed in this study. Assefa *et al* at Gondar University Hospital in Ethiopia found retinal microvasculopathy in 24% of patients which is less than that found in this study (8). Ndoye *et al* found that patients with CD4 counts between 0 and 200 had macular oedema, hyalitis, cotton-like nodules, retinal uveitis, and microangiopathy, while those with higher CD4 counts had none of these ocular lesions. The only ocular lesion in patients with CD4 counts between 200 and 400 was ophthalmic herpes zoster in Ndoye's study (5).

Anterior segment manifestations were seen in 36.5% of patients, the most notable being a greyish fibrous membrane attached to the iris mostly near the pupillary margin (18.5%), followed by active iridocyclitis (5.5%). Similarly Nwosu *et al* in Nigeria found iridocyclitis in 4% of the patients. The membrane could be due to old resolving immune recovery uveitis.

Mvogo *et al* in Cameroon found anterior segment abnormalities in 30% of their HIV/AIDS patients (4). The principal lesions of the anterior segment in their study were herpetic keratitis (10.5%) and HZO (12.3%). In this study membranes in the papillary area were the most predominant feature in the anterior segment. This could be due to frequent recurrent uveitis episodes which have been reported as immune recovery ocular inflammation in HAART patients. Herpes Zoster Ophthalmicus accounted for 6% of the ocular findings in all HIV/AIDS patients in this study. Most of them had both lid involvement and corneal involvement. The highest prevalence of HZO in HIV patients was reported by Nwosu *et al* in Nigeria at 48%. Msosa *et al* found HZO in 0.8% of all patients attending an eye clinic at Kenyatta National Hospital in Kenya regardless of their HIV status (10). Ndoye *et al* reported an HZO prevalence of 8.5% in HIV/AIDS patients in Dakar, Senegal (6). This is similar to the findings noted in HIV/AIDS patients at AMPATH clinic in this study.

Adnexal manifestations were present in 26% of our patients and the main findings were squamous cell carcinoma (6.5%), HZO (6%), Kaposi Sarcoma (5%), conjunctival microvasculopathy (4.5%), molluscum contagiosum (2.5%) and suspicious conjunctival growth (1.5%). The lower prevalence of microvasculopathy noted in this study could be due to the fact that most of the patients were on HAART for a longer duration and the consequent decrease in the viral load may lead to a decline in the vasculopathy.

The prevalence of squamous cell carcinoma in this study was comparable to findings by Chisi *et al*. They noted a prevalence of proven conjunctiva SCC of 7.8 % in HIV patients (11). Ten of the SCC were diagnosed clinically while three had histological confirmation. Guech, Ongey *et al* in the USA found a significantly increased risk for squamous cell carcinoma in patients with HIV/AIDS (12).

Neurophthalmic findings were seen in 11 patients and included optic atrophy (3 patients), papilloedema (4 patients) and papilitis (4 patients). Assefa *et al* found neuro-ophthalmologic disorders in 9.6% in their HIV/AIDS patients which is similar to this study (8). Two cases of papilloedema and two cases of papillitis were attributed to cryptococcal meningitis based on the clinical appearance and context. However, no other specific causes for neuro-ophthalmologic findings could be established. This is similar to other studies from comparable settings where limited diagnostic capacities often prevent establishing exact causes. These infections are due to the immunosuppression of HIV.

Systemic manifestations of HIV/AIDS were seen in 81 patients with TB (53.1%) and oro-pharyngeal candidiasis (23.5%) being the commonest. In Malawi, Beare *et al* found TB in 43% of the patients with HIV/AIDS (13). They noted choroidal granulomas in 3% of patients with systemic TB. No choroidal granulomas were found in this study. There was no significant association between systemic diseases and ocular manifestations. However, a number of patients with TB and oro-pharyngeal candidiasis were also noted to have ocular manifestations but this was not statistically significant.

In this study most patients were in HIV/AIDS stage I (36%), followed by stage III (9.5%), stage II (23%) and stage IV (11.5%) (Figure 6). Patients in stage IV had the highest prevalence of ocular manifestations (95.7%) followed by patients in stage III (91.5%). The least prevalence was noted in stage I (66.7%). This relation was statistically significant and suggests that the magnitude of the ocular involvement increases with severity of the HIV/AIDS disease (Table 1). The higher magnitude of ocular manifestations in stage I demonstrates that ocular manifestations may occur at any CD4 count. Most of the manifestations in this stage were non-blinding. Assefa *et al* in their study from Ethiopia reported 90% of the patients in clinical stage III and IV. Of these, 60% had at least one ocular manifestation (8).

CD4 T lymphocyte counts have previously been said to be a reliable predictor of ocular complications of HIV infections (4). This study found that patients with CD4 count less than 100 cells/ml had higher rate (95.5%) of ocular manifestations (p=0.04).

However the study showed no linear association between ocular adnexal findings, ocular anterior segment findings and neuro-ophthalmic findings with the level of CD4 count, but demonstrated a positive association between posterior segments findings (p=0.04).

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