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BRIEF REPORT

Ocular manifestations of HIV/AIDS among patients who have not received highly active antiretroviral therapy: brief report

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A spectrum of ocular manifestations is associated with the decrease in CD4+ (T-cell) count to less than 200 cells/uL in patients with acquired immunodeficiency syndrome (AIDS).[1] Ocular manifestations are frequently caused by opportunistic infections—such as cytomegalovirus (CMV) retinitis, varicella-zoster virus (VZV) retinitis, and mycobacterium avium complex (MAC) infection—and neoplasms such as Kaposi sarcoma and lymphoma.[2] The ocular manifestations of HIV may involve the adnexa, anterior and posterior segments, and/or the orbit.[3,4]

Opportunistic infections differ across different parts of the world, and even among Asian countries, due to varying local prevalence of opportunistic agents.[5] Further, the patterns of ocular disease in HIV patients vary in different regions due to differences in timing of deaths in developed and developing countries, HIV subtypes, and sociocultural factors affecting testing and therapy.[6] With the introduction of highly active antiretroviral therapy (HAART), the patterns and prevalence of ocular manifestations of HIV/AIDS have changed considerably.[2,7,8] From 4,300 in 2010, the number of Filipinos infected with HIV rose to 10,500 in 2016.[9] As more patients are diagnosed with HIV infection and AIDS, there is greater need to determine the morbidity rate and identify factors that increase the likelihood of having ocular manifestations of these conditions.

We did this study to determine the presence of ocular manifestations of HIV/AIDS among patients who have not received highly active antiretroviral therapy. We also wanted to identify demographic and clinical factors associated with having any ocular manifestations of HIV/AIDS.

We did a cross-sectional study from January to November 2017 among patients referred by the HIV/AIDS Core Team (HACT) Clinic of Southern Philippines Medical Center (SPMC) to the SPMC Ophthalmology Outpatient Clinic for routine eye examination. The clinic receives an average of 20 patients per month as referrals from the HACT Clinic of SPMC.

Patients aged 18 years old and above who tested positive for HIV infection by an HIV screening test (with or without a confirmatory test) and who have not received HAART were eligible for inclusion into the study. We excluded patients who could not tolerate the sitting position for the slit-lamp examination—i.e., patients who were intubated or otherwise non-ambulatory.

We estimated the minimum sample size for this study using StatCalc from Epi Info 7.1.4.0 based on the assumption that 63.6% of patients with CD4+ count <200cells/uL

Table 1 Sociodemographic and clinical profile of patients

Characteristics	Values n=75
Mean age ± SD, *years*	28.75 ± 7.18
Sex, *frequency (%)*	
Male	72 (96.00)
Female	3 (4.00)
Systemic comorbidities, *frequency (%)**	
Pulmonary tuberculosis	18 (24.00)
Pneumonia	7 (9.33)
Herpes zoster	5 (6.67)
Diabetes	2 (2.67)
Gonorrhea	2 (2.67)
Syphilis	2 (2.67)
Hypertension	1 (1.33)
Anxiety/depression	1 (1.33)
Mitral valve prolapse	1 (1.33)
Kaposi sarcoma	1 (1.33)
Psoriasis	1 (1.33)
Non-Hodgkin's lymphoma	1 (1.33)
Candida esophagitis	1 (1.33)
Bronchial asthma	1 (1.33)
Ocular comorbidities, *frequency (%)**	
Strabismus	2 (2.67)
Diabetic retinopathy	1 (1.33)
Pinguecula	1 (1.33)
Chlamydial conjunctivitis	1 (1.33)
Exotropia	1 (1.33)
Fungal keratitis	1 (1.33)

* One patient may have more than one comorbidity.

Table 2 Clinical characteristics of the 150 eyes examined

Characteristics	Values n=150
Mean visual acuity ± SD, *logMAR**	0.34 ± 0.21
Visual performance, *frequency (%)*	
Normal	143 (95.33)
Moderately low vision	4 (2.67)
Severe low vision	1 (67)
Near blindness	2 (1.33)
Mean intraocular pressure ± SD, *mmHg*	13.37 ± 3.37
10-21	140 (93.33)
<10	10 (6.67)
Patency of iridocorneal angle, *frequency (%)*	
Open angle	150 (100)
Closed angle	0 (0)
Tear break-up time, *frequency (%)*	
<10 seconds	13 (8.67)
≥10 seconds	137 (91.33)

* logMAR=logarithm of the minimum angle of resolution

and 23.6% of patients with CD4+ count of ≥200cells/uL have some form of ocular manifestations related to HIV/AIDS.[7] In a computation for odds ratio to determine the association of selected clinical factors with any ocular manifestations carried out at a 5% level of significance, a minimum sample size of 63 will have 80% power of rejecting the null hypothesis, if the alternative holds.

After obtaining the informed consent of the participants, we gathered their baseline demographic and clinical data including age, sex, and systemic and ocular comorbidities. The baseline CD4+ counts were also recorded and were categorized as low when <200 cells/uL, or high when ≥200 cells/uL. We classified patients as having 'HIV infection' when their baseline CD4+ counts were ≥200 cells/uL and they do not have any AIDS-defining conditions. We classified patients as having 'AIDS' when they either have any AIDS-defining conditions (regardless of CD4+ counts) or CD4+ counts of <200 cells/uL (regardless of the presence or absence of any AIDS-defining conditions).[10 11] We also recorded our findings on routine eye examination including visual acuity, intraocular pressure, patency of the iridocorneal drainage angle, and tear break-up time (TBUT). To determine the presence of and ocular structures (i.e., anterior segment, posterior segment, and/or ocular adnexa) involved in ocular manifestations of HIV/AIDS, we performed thorough slit-lamp biomicroscopy, posterior segment examination, and ocular adnexal examination.

We summarized continuous variables as means and standard deviations and compared them using t-test. We summarized categorical variables as frequencies and percentages and compared proportions using chi-square test or Fisher's exact test. A two-tailed p-value of <0.05 was considered significant. Association of variables were expressed as cross-sectional odds ratios (OR) and their 95% confidence intervals. We performed univariate logistic regression to determine the unadjusted association of demographic or clinical factors with any ocular manifestations. We used Epi Info™ 7.2.1 for all our statistical tests.

A total of 75 patients were recruited into the study. Table 1 shows the demographic and clinical profiles of patients. There were 72/75 (96%) males and 3/75 (4%) females, and the mean age of the patients was 28.75 ± 7.18 years. At baseline, 14/75 (18.67%) had HIV infection alone, while 61/75 (81.33%) had AIDS (HIV infection with either CD4+ count <200 cells/uL or an AIDS- defining condition). The most common systemic comorbidities were pulmonary tuberculosis (18/75, 24.00%), pneumonia (7/75, 9.33%), and herpes zoster (5/75, 6.67%), while the most common ocular comorbidity was strabismus (2/75, 2.67%).

Table 2 shows the profile of the individual eyes examined. A total of 150 eyes were included in this summary. The mean visual acuity was 0.34 ± 0.21 logMAR. Majority of the eyes (143/150, 95.33%) had normal visual acuity, while 2/150 (1.33%) had near total blindness. The mean intraocular pressure was 13.37 ± 3.37 mmHg. All of the eyes had open iridocorneal drainage angle. Most eyes (137/150, 91.33%) had a tear break-up time of ≥10 seconds.

Among the 75 participants, the mean CD4+ count was 143.28 ± 218.75 cells/uL, and 56 (74.67%) had CD4+ counts <200

Table 3 CD4+ profiles

Characteristics	All n=75	With ocular manifestations n=23	Without ocular manifestations n=23	p-value
Mean age ± SD, *cells/uLs*	143.28 ± 218.75	102.78 ± 258.70	161.19 ± 198.74	0.2894
Low CD4+ count (<200 cells/uLs)	56 (74.67)	21 (91.30)	35 (67.31)	0.0420*†

* logMAR=logarithm of the minimum angle of resolution.
† Fisher's exact test.

Table 4 Distribution of ocular manifestations per CD4+ count category

	Total n=75	Low CD4+ count n=56	High CD4+ count n=19
At least one ocular manifestation, *frequency (%)**	23 (30.67)	21 (37.50)	2 (10.53)
Anterior segment, *frequency (%)*	9 (12.00)	7 (12.50)	2 (10.53)
Keratoconjunctivitis sicca	7 (9.33)	7 (12.50)	0 (0.00)
Keratitis	2 (2.67)	2 (3.57)	0 (0.00)
Posterior synechiae	2 (2.67)	0 (0.00)	2 (10.53)
Corneal scar	1 (1.33)	1 (1.79)	0 (0.00)
Posterior segment, *frequency (%)*	17 (22.67)	16 (28.57)	1 (5.26)
HIV retinopathy	13 (17.33)	12 (21.43)	1 (5.26)
CMV retinitis	3 (4.00)	3 (5.36)	0 (0.00)
Chronic retinal necrosis	1 (1.33)	1 (1.79)	0 (0.00)
Chorioretinal scar	1 (1.33)	1 (1.79)	0 (0.00)
Ocular adnexa, *frequency (%)*	6 (8.00)	6 (10.71)	0 (0.00)
Blepharitis	4 (5.33)	4 (7.14)	0 (0.00)
Molloscum contagiosum	1 (1.33)	1 (1.79)	0 (0.00)
Verruca vulgaris	1 (1.33)	1 (1.79)	0 (0.00)
Madarosis	1 (1.33)	1 (1.79)	0 (0.00)

* One patient may have more than one ocular manifestation.

Table 5 Association of selected patient factors and any ocular manifestation

	Unadjusted cross-sectional odds ratio (95% CI)	p-value
Age ≤35 years old	0.4407 (0.1295 to 1.5002)	0.1899
Male	0.8800 (0.0758 to 10.2097)	0.9186
Pulmonary tuberculosis	0.8333 (0.2579 to 2.6928)	0.7606
Pneumonia	3.4320 (0.7015 to 16.7912)	0.1279
Herpes zoster	0.5462 (0.0577 to 5.1707)	0.5980
Diabetes	2.3179 (0.1386 to 38.7519)	0.5586
Syphilis	2.3179 (0.1386 to 38.7519)	0.5586
Low CD4+ count	5.0955 (1.0693 to 24.2818)	0.0409*

* Significant at p<0.05.

cells/uL (low), while 19 (25.33%) had counts ≥200 cells/uL (high). A total of 23 (30.67%) patients had one or more ocular manifestations of HIV/AIDS. Table 3 shows the CD4+ profiles of the participants, with comparisons between those with ocular manifestations and those without. The mean CD4+ counts between the two groups were comparable. However, the proportion of patients with low CD4+ count was significantly higher among those with ocular manifestations (21/23, 91.30%) than among those without ocular manifestations (35/52, 67.31%; p=0.0420).

Table 4 shows the distribution of specific ocular manifestations, classified according to CD4+ count category (low versus high). Of the 75 patients, 56 (74.67%) had low CD4+ counts (<200 cells/uL). Among patients with low CD4+ counts 21/56 (37.5%) had ocular manifestations, while among those with high CD4+ counts 2/19 (10.53%) had ocular manifestations.

The results of the univariate logistic regression, showing the association of specific demographic and clinical factors and any ocular manifestations, are in Table 5. Only low CD4+ count had significant association with the presence of any ocular manifestation (OR=5.0955; p=0.0409).

The findings in this study are applicable to most patients diagnosed with HIV infection or AIDS prior to HAART. Males and females were equally represented in our study, and the

age range of patients we included was quite broad. Clinical characteristics (e.g., ocular characteristics, systemic and ocular comorbidities, and CD4+ count categories) were also well represented in this study.

In summary, we found out in this cross-sectional study that ocular manifestations of HIV/AIDS were present in 30.67% of patients who have not received highly active antiretroviral therapy. The posterior segment of the eye was the most affected structure, and HIV retinopathy was the most common ocular manifestation. Having a low CD4+ count significantly increased the odds ratio of having ocular manifestations of HIV/AIDS. Early detection of ocular manifestations of HIV/AIDS is important since these ocular morbidities may compromise vision, or may even signify a more serious systemic illness that could highly affect the prognosis of HIV infection or AIDS.

Contributors
BJTC and RCG both had substantial contributions to the study design, and to the acquisition, analysis and interpretation of data. BJTC and RCG wrote the original draft and subsequent revisions, and both authors reviewed, edited, and approved the final version of the manuscript. BJTC and RCG both agreed to be accountable for all aspects of the work.

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Ethics approval
This study was reviewed and approved by the Department of Health XI Cluster Ethics Review Committee (DOH XI CERC reference P08111401).

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