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Ophthalmic Disease Prevalence and Incidence among People Living with HIV in AFRICOS

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Abstract

Ophthalmic disease in people living with HIV (PLWH) and at-risk controls in Sub-Saharan Africa was evaluated. PLWH were more likely to have ophthalmic disease at enrollment, but there was no difference in incidence once enrolled.

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Report

Sub-Saharan Africa is disproportionately affected by the human immunodeficiency virus (HIV) pandemic, with approximately 26 million people living with HIV (PLWH) and 1.1 million new cases annually.[1] Blindness is experienced by 5–25% of PLWH in the developing world at some point during their illness.[2] Over 80% of visual impairment in this region could be avoided or cured, but prevention and treatment require ophthalmological expertise that is rarely available in Sub-Saharan Africa.[3] Although access to ophthalmic care is challenging for PLWH in Sub-Saharan Africa, access to modern antiretroviral therapy (ART) has improved over the last 15 years as has the timeliness of ART initiation after HIV diagnosis.[4]

Although over two-thirds of PLWH worldwide reside in Sub-Saharan Africa, there is limited data on HIV-related ophthalmic disease in this region in the era of widely available ART. AFRICOS is a prospective, HIV-focused cohort study that enrolls adults living with and at risk for HIV at twelve clinics in Kenya, Uganda, Tanzania, and Nigeria.[5]

AFRICOS was approved by the institutional review boards of the Walter Reed Army Institute of Research, Makerere University School of Public Health, Kenya Medical Research Institute, Tanzania National Institute of Medical Research, and Nigerian Ministry of Defense approved this study. The investigators of this study have adhered to the policies for protection of human participants as prescribed in AR 70–25. Each participant provided informed consent that was documented with a signature or fingerprint if illiterate.

Every six months, participants underwent a medical history that included medical record extraction, physical examination, and clinical assessments as previously described.[5] Ophthalmic disease cases/events were defined by ICD-10 codes (W43.2, W47.9, C69.0, H54.0, H30.9, A71, H44.1, H54.1, H10, H00, H26.9) or results of screening for cytomegalovirus retinitis (CMV) and Kaposi’s Sarcoma (KS) (including KS of the conjunctiva and/or eyelid) as part of the WHO HIV staging.

Enrollment characteristics were compared between participants with and without prevalent and/or incident ophthalmic diseases. Incidence rates were calculated as the number of new ophthalmic diagnoses divided by person-years (PY) of follow-up. Confidence intervals (CIs) were calculated using the quadratic approximation to the Poisson log likelihood for the log-rate parameter. P-values were calculated using Fisher’s exact tests for categorical and Wilcoxon rank-sum tests for continuous variables. Cox proportional hazard models were used to estimate hazard ratios (HRs) and 95% CIs for factors potentially associated with a first incident ophthalmic diagnosis, including time updated CD4 counts, HIV viral load, and ART regimen class. For incidence rates by diagnosis code, participants could contribute one incident case to each unique diagnosis, with one participant being diagnosed with 2 different ophthalmic diseases during follow-up. There was one participant with prevalent ophthalmic disease at enrollment who was included in the incidence calculations and Cox proportional hazard models. All tests were two-sided and a p-value less than 0.05 was considered statistically significant. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC) and Stata version 15.0 (StataCorp, College Station, Texas).

Among 3503 enrolled participants, PLWH had a higher prevalence of ophthalmic diagnoses than participants at risk for HIV [113/2918(3.9%) vs 2/585 (0.3%); p<0.001] (Table 1). During the study period, 93 new cases of ophthalmic disease were diagnosed in PLWH and 19 in participants at risk for HIV. The incidence of ophthalmic disease was not significantly different by HIV status (Table 2, p=0.45). Conjunctivitis was the most common diagnosis at enrollment (89.9% of diagnoses) and among incident cases (86.8% of diagnoses; Supplemental Table 1). There were no cases of CMV retinitis or other AIDS-defining ocular infections or malignancies.

Baseline characteristics of PLWH and HIV at-risk participants were collected (Supplemental Table 2). Factors independently associated with increased risk of incident ophthalmic disease among PLWH included being 50 years or older as compared to those 18–29 (HR 1.03; 95% CI 1.01–1.05, p=0.001; Supplemental Table 3). Lower risk was observed with a CD4 count of 200–499 compared to <200 (HR 0.70; 95% CI 0.52–094, p=0.016) and NRTI/NNRTI (HR 0.56; 95% CI 0.32–0.96, p = 0.036) or NRTI/I (HR 0.53; 95% CI 0.30–0.96, p=0.038) regimens as compared to ART naïve participants.

Ophthalmic disease was less common in our study than in others from sub-Saharan Africa, which have mostly observed a prevalence of 12–48% and as high as 60–70% in patients with AIDS.[6] As compared to older studies, participants in AFRICOS are able to obtain treatment earlier in the course of their disease, potentially reducing the prevalence of severe ocular pathologies associated with advanced HIV disease. The vast majority of AFRICOS participants were on ART and less than 20% had an AIDS-defining CD4 count. HIV-associated ophthalmic disease is often transient and asymptomatic, and patients often do not report symptoms and have satisfactory visual acuity. Thus, ophthalmic disease is easy to miss unless a dilated ophthalmic exam is performed by qualified personnel, visual acuity testing is performed, and the patient is asked about specific ocular symptoms.

Nearly 90% of prevalent and incident ophthalmic disease in this study was conjunctivitis. In the post-ART era, studies have shown higher prevalence and incidence of external eye conditions (i.e. blepharitis, pterygium, conjunctivitis and keratoconjunctivitis sicca) in PLWH.[7] The increase in external eye conditions may be due to HIV-induced immunosuppression leading to reduced ability to control normal bacterial flora in the cutaneous glands of the eye lids, destruction of the lacrimal glands and damage to the conjunctiva from HIV-mediated immune activation and lymphocytic infiltration.

Ophthalmic disease was not a primary endpoint of the AFRICOS cohort, so a full ophthalmic history, visual acuity testing and dilated ophthalmic exam were not routinely performed, limiting our ability to detect asymptomatic or mild ophthalmic disease. Comparison with prior African studies is challenging, since many lacked a comparator group without HIV or without ophthalmic diagnoses, enrolled participants only with advanced HIV disease or specific ART status, or examined only specific ocular disease processes.

In conclusion, the prevalence of ophthalmic disease in PLWH in post-ART era Sub-Saharan Africa was lower than previously reported, but significantly higher than in individuals at risk

for HIV. After study enrollment, there was no difference in ophthalmic disease incidence between participants with and without HIV, suggesting that improved access to HIV-related care may reduce ophthalmic disease risk. Conjunctivitis was the most common diagnosis while severe ocular infections classically seen in patients with advanced HIV were exceptionally rare. Further prospective analysis to better understand the incidence and prevalence of ophthalmic disease and risk factors in PLWH in Sub-Saharan Africa is needed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Prevalence of eye disease at enrollment and incidence of eye disease between January 21 2013 and September 1 2019.

Prevalence of eye disease	**All**	**PLWH**	**HIV-uninfected**	
eye disease at enrollment	115	113	2	
participants enrolled	3503	2918	585	
prevalence at enrollment	3.3%	3.9%	0.3%	
				p<0.001
Incidence of eye disease	**All**	**PLWH**	**HIV-uninfected**	
new cases of eye disease	112	93	19	
Incidence rate (per 1000 person-yrs)	10.969	10.652	12.841	
95% CI Lower (per 1000 person-yrs)	9.115	8.693	8.191	
95% CI Upper (per 1000 person-yrs)	13.201	13.053	20.131	
				p=0.4526