AMERICAN ACADEMY™
OF OPHTHALMOLOGY

# Ophthalmic Manifestations and Causes of Vision Impairment in Ebola Virus Disease Survivors in Monrovia, Liberia

*Jessica G. Shantha, MD,*[1] *Ian Crozier, MD,*[2] *Brent R. Hayek, MD,*[1] *Beau B. Bruce, MD, MPH,*[1,3,4] *Catherine Gargu,*[5] *Jerry Brown, MD,*[6] *John Fankhauser, MD,*[6] *Steven Yeh, MD*[1]

***Purpose:*** To describe the ocular findings, visual impairment, and association of structural complications of uveitis with visual impairment in a cohort of survivors of Ebola virus disease (EVD) in Monrovia, Liberia.

***Design:*** Retrospective, uncontrolled, cross-sectional study.

***Participants:*** Survivors of EVD who were evaluated in an ophthalmology clinic at Eternal Love Winning Africa (ELWA) Hospital in Monrovia, Liberia.

***Methods:*** A cohort of EVD survivors who underwent baseline ophthalmic evaluation at ELWA Hospital were retrospectively reviewed for demographic information, length of Ebola treatment unit (ETU) stay, visual acuity (VA), and ophthalmic examination findings. For patients with uveitis, disease activity (active vs. inactive) and grade of inflammation were recorded according to Standardization of Uveitis Nomenclature criteria. The level of VA impairment was categorized according to World Health Organization classification for VA impairment as follows: normal/mild, VA 20/70 or better; moderate, VA 20/70−20/200; severe, VA 20/200−20/400; blindness, VA <20/400. Visual acuity, length of ETU stay, and structural complications were compared between EVD survivors with and without uveitis. Structural complications associated with moderate VA impairment or poorer were analyzed.

***Main Outcome Measures:*** Frequency of ocular complications including uveitis and optic neuropathy in EVD survivors, level of VA impairment in EVD survivors with uveitis, and structural complications associated with VA impairment in EVD survivors.

***Results:*** A total of 96 survivors of EVD were examined. A total of 21 patients developed an EVD-associated uveitis, and 3 patients developed an EVD-associated optic neuropathy. Visual acuity was blind (VA >20/400) in 38.5% of eyes with uveitis. Anatomic subtypes of uveitis included anterior, posterior, and panuveitis in 2, 13, and 6 patients, respectively. Examination findings associated with at least moderate visual impairment by World Health Organization criteria (VA <20/70) included keratic precipitates ($P < 0.002$), posterior synechiae ($P < 0.002$), vitritis ($P < 0.005$), and chorioretinal scars ($P < 0.02$).

***Conclusions:*** Survivors of EVD are at risk for uveitis, which may lead to secondary structural complications, visual impairment, and blindness. Eye care resources should be mobilized for EVD survivors in West Africa because of the frequency of this spectrum of disease complication and its potential for severe VA impairment and blindness. *Ophthalmology 2016;■:1−8 © 2016 by the American Academy of Ophthalmology*

The international community has witnessed the largest Ebola virus disease (EVD) outbreak in history, predominantly in the West African countries of Guinea, Liberia, and Sierra Leone, which have the highest rates of transmission. More than 28 600 confirmed, probable, or suspected EVD cases were identified during this outbreak, and approximately 37% of cases occurred in Liberia; specifically, there were more than 10 000 cases of EVD resulting in 4809 deaths.[1] The magnitude of the outbreak has lent itself to the largest cohort of EVD survivors in history. As the acute EVD outbreak has subsided, increased attention has shifted to ongoing Ebola survivor care needs.

Before this outbreak, there were 23 EVD outbreaks with 2345 laboratory-confirmed cases and 1546 deaths documented throughout Africa. These previous outbreaks have provided limited information on the long-term sequelae after EVD. The post-EVD syndrome, which develops during EVD convalescence, consists of fatigue, arthralgias, myalgias, neurologic complications, abdominal pain, sensorineural hearing loss, increased risk of miscarriage, psychosocial stressors, and vision loss.[2−4] Post-EVD syndrome has been reported with greater frequency given the historic magnitude of the recent Ebola outbreak.

Ocular complications in patients with EVD have been observed during acute disease and convalescence. During active Ebola virus infection, a bilateral viral conjunctivitis with or without subconjunctival hemorrhage is typical, and acute vision loss has been described in some patients, but the cause of vision loss has not been fully characterized.[5] Ocular manifestations in EVD survivors during



http://dx.doi.org/10.1016/j.ophtha.2016.10.011
ISSN 0161-6420/16

convalescence were first reported in the 1995 Kikwit outbreak. In 4 EVD survivors, a spectrum of uveitis ranging from anterior to posterior disease developed 42 to 72 days after EVD onset.[5] During the most recent outbreak, 2 repatriated physicians who contracted EVD while working in West Africa developed acute, sight-threatening uveitis after recovering from EVD.[6,7]

More detailed observations from the recent West African outbreak have provided additional information about ophthalmologic sequelae. Specifically, Mattia et al[8] described uveitis, arthralgias, and auditory symptoms in 18%, 26%, and 24% of survivors, respectively, from the Port Loko District, Sierra Leone, during convalescence. In this cohort, a low reverse transcription polymerase chain reaction cycling threshold during acute disease was an independent predictor of the development of uveitis.[8] Other surveys of EVD survivors report a wide range of symptoms, such as headache, anorexia, abdominal pain, fatigue, short-term memory loss, and blurred vision.[9,10] In another cohort of EVD survivors in Freetown, Sierra Leone, 34% of patients were diagnosed with uveitis. Eye injection/redness during acute EVD was found to be a risk factor for uveitis development. Other common ocular diseases in these patients included conjunctivitis, cataract, and glaucoma.[11]

Eye symptoms are frequent among survivors, and EVD-associated uveitis is an urgent diagnosis with potential interventions that may ultimately affect visual outcome and quality of life in West Africa survivors. We report the detailed ophthalmic manifestations, structural complications, and associated visual acuity (VA) impairment in recovered patients with EVD who were evaluated at the Eternal Love Winning Africa (ELWA) Hospital in Monrovia, Liberia.

## Methods

### Study Design and Population

A retrospective, uncontrolled, cross-sectional study was performed on EVD survivors who underwent ophthalmic examination at the ELWA Hospital EVD Survivor Clinic in Monrovia, Liberia. This study was approved by the Emory University Institutional Review Board and the University of Liberia National Institutional Review Board and follows the tenets set forth by the Declaration of Helsinki.

Patients were determined to be EVD survivors by providing the examiners with an Ebola survivor certificate that is given to each patient upon discharge from an Ebola treatment unit (ETU). Survivors were treated in the following ETUs in Liberia: Foya, ELWA 2, ELWA 3, Medecins Sans Frontieres, Bong County, US Public Health Service, Ministry of Defense, Modi, John F. Kennedy, Gbanga, Congo, Medecins Sans Frontieres B, Bomi, Island Clinic, and Firestone.

An ophthalmology clinic was established in partnership with Emory Eye Center health care providers and the ELWA Hospital in April 2015. Patients were evaluated, treated, or referred as needed by examining ophthalmologists.

### Infection Control/Personal Protective Equipment

All patients underwent an initial general medical health screening by health care professionals wearing personal protective equipment that included a face shield, gown, gloves, and rubber boots. Patients were screened for fever with infrared thermometers and a questionnaire on symptoms of Ebola. Any patient with active EVD symptoms (diarrhea, vomiting, headache, abdominal pain) or elevated temperature greater than 100.4°F (38.0°C) failed screening and were not examined that day by the ophthalmic providers until a medical evaluation had been conducted. In the outpatient eye clinic, providers wore fluid-impervious gowns and gloves when providing patient care. All equipment was cleaned with alcohol swabs between each examination.

### Data Collection

The medical records of 96 EVD survivors evaluated in April 2015 were retrospectively reviewed. Data collected included medical and ocular history, ETU admit and discharge dates, ocular and systemic symptoms, ophthalmic examination consisting of corrected VA or pinhole VA (Snellen VA or tumbling "E" chart), pupil examination, extraocular motility, confrontational visual fields, slit-lamp examination, intraocular pressure (IOP) measurement (Reichert Technologies, Depew, NY), and dilated fundus examination with indirect ophthalmoscopy.

Demographic data recorded included ethnicity, age, and gender. Ocular symptoms recorded were eye pain, tearing, redness, difficulty with near vision, light sensitivity, floaters, and blurred vision. A full review of symptoms was performed, specifically documenting the presence of patient self-reported fatigue, joint pain, hearing loss, and hair loss.

Uveitis was classified on the basis of the anatomic location of inflammation following the Standardization of Uveitis Nomenclature guidelines.[12] Active uveitis was defined as the presence of inflammation (cell/flare) in the anterior chamber (i.e., trace cell or greater) or vitreous haze with/without keratic precipitates, corneal infiltrates, vascular sheathing, and retinal or choroidal infiltrates.

Inactive disease was characterized by signs of previous inflammation, including pigmented keratic precipitates, corneal scars, posterior synechiae, condensed vitreous opacities, and chorioretinal scars.

Ebola-associated eye disease was defined as eye disease/findings with vision loss or symptoms that occurred during acute Ebola virus infection or after discharge from an ETU that was not related to trauma, prior documented illness/infection, or congenital disease. Ocular hypertension was defined as an IOP >21 mmHg, and hypotony was defined as an IOP <5 mmHg.

### Main Outcome Measures

The primary outcome measured was the level of visual impairment in EVD survivors. Secondary outcomes evaluated included anatomic diagnoses leading to visual impairment in EVD survivors, structural complications identified in EVD survivors, and the association of specific anatomic features and structural complications with vision loss.

### Statistical Analysis

Statistical analysis was performed with R 3.2.4. Descriptive data were summarized, including demographic data and ocular and systemic symptoms. An unpaired $t$ test was used to compare the number of days in an ETU and baseline VA in patients with and without uveitis. The Fisher exact test was used for categoric variable comparisons. Visual impairment was categorized by the World Health Organization's classification: normal or mild visual impairment, VA ≥20/70; moderate visual impairment, VA 20/70−20/200; severe visual impairment, VA 20/200−20/400; and blindness, VA >20/400.[13] Visual acuities were converted to