Early clinical sequelae of Ebola virus disease in Sierra Leone: a cross-sectional study

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Summary

Background **Limited data are available on the prevalence and predictors of clinical sequelae in survivors of Ebola virus disease (EVD). The EVD Survivor Clinic in Port Loko, Sierra Leone, has provided clinical care for 603 of 661 survivors living in the district. We did a cross-sectional study to describe the prevalence, nature, and predictors of three key EVD sequelae (ocular, auditory, and articular) in this cohort of EVD survivors.**

Methods **We reviewed available clinical and laboratory records of consecutive patients assessed in the clinic between March 7, 2015, and April 24, 2015. We used univariate and multiple logistic regression to examine clinical and laboratory features of acute EVD with the following outcomes in convalescence: new ocular symptoms, uveitis, auditory symptoms, and arthralgias.**

Findings **Among 277 survivors (59% female), median age was 29 years (IQR 20–36) and median time from discharge from an EVD treatment facility to first survivor clinic visit was 121 days (82–151). Clinical sequelae were common, including arthralgias (n=210, 76%), new ocular symptoms (n=167, 60%), uveitis (n=50, 18%), and auditory symptoms (n=67, 24%). Higher Ebola viral load at acute EVD presentation (as shown by lower cycle thresholds on real-time RT-PCR testing) was independently associated with uveitis (adjusted odds ratio [aOR] 3·33, 95% CI 1·87–5·91, for every five-point decrease in cycle threshold) and with new ocular symptoms or ocular diagnoses (aOR 3·04, 95% CI 1·87–4·94).**

Interpretation **Clinical sequelae during early EVD convalescence are common and sometimes sight threatening. These findings underscore the need for early clinical follow-up of survivors of EVD and urgent provision of ocular care as part of health systems strengthening in EVD-affected west African countries.**

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See Comment page 270

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Introduction

The Ebola virus disease (EVD) outbreak in west Africa is the largest in history. As of November, 2015, over 28 500 EVD cases have been reported with an estimated 15 000 survivors.[1] Community-led survivor networks have alerted health-care providers to a variety of convalescent symptoms, including vision and hearing loss and arthralgia.[2–4]

Understanding of the nature, timing, and prevalence of EVD sequelae remains limited.[5–13] Disabling sequelae, including ocular, auditory, and arthritic symptoms, have been described in small studies from previous outbreaks.[7,9–11,13] In the current outbreak, one qualitative study of 100 survivors in Sierra Leone reported blurred or partial loss of vision in convalescence but did not quantify these sequelae.[2] Surveys of 105 survivors in Guinea[14] and of 81 survivors in Sierra Leone[15] noted frequent musculoskeletal pain[14,15] and visual problems;[15] neither study included a clinical examination of survey participants. No studies from the west African outbreak have examined possible relations between features of acute EVD and the frequency or severity of clinical sequelae. Therefore, we did a cross-sectional study to describe the prevalence, nature, and predictors of three key EVD sequelae (ocular, auditory, and articular) in a large cohort of survivors of EVD in Port Loko district, Sierra Leone.

Methods

Study setting

By Nov 12, 2015, 1485 EVD cases were reported from the rural district of Port Loko (population 572 369), with 661 survivors according to the Sierra Leone Association for Ebola Survivors registry.[16] Before Nov 30, 2014, some patients were referred for care in Ebola treatment units (ETUs) outside the district, since ETU scale-up was still underway in Port Loko. After Nov 29, 2014, 90% of patients with EVD in Port Loko received care at one of three ETUs (Maforki, Mathaska, and Lunsar) in the district. The Port Loko EVD Survivor Care Clinic was established on March 7, 2015, at the Baptist Eye Hospital Lunsar as a clinical partnership between Partners in Health (PIH), the PIH-supported EVD Survivor Network,

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Research in context

Evidence before this study

A MEDLINE search on the prevalence of post-Ebola virus disease (EVD) clinical sequelae using search terms "Ebola" and "survivor OR sequelae OR convalescen*" yielded 227 unique citations published by Nov 12, 2015. There were no language restrictions. Excluding case reports, commentaries, and expert reviews, nine studies (case series, cohorts, and cross-sectional surveys) provided clinical information post-Ebola sequelae, including three from the current west Africa outbreak. Only six studies quantify the prevalence of clinical sequelae, of which four explored early clinical sequelae in 240 survivors of Ebola within 3–4 months of convalescence. To date, measurement of clinical sequelae was based on a clinical examination in only 57 patients (from two studies of previous outbreaks), and only four patients in these studies received a complete ophthalmological examination (visual acuity, slit-lamp, dilated fundoscopy). The largest (n=105) published study of early EVD clinical sequelae was based on self-reported symptoms without a clinical examination, with restricted questions on ocular and auditory symptoms that were self-reported in none of the 105 survivors of EVD. None of the studies examined the predictors of developing early or late EVD clinical sequelae.

Added value of this study

This study's systematic clinical examination of EVD sequelae includes the largest representative sample of west African survivors of EVD from the 2014–15 outbreak. Unlike studies from previous clinical cohorts, the clinical and laboratory data were drawn from a more representative sample, with detailed and protocol-defined clinical charting and clinical examination, and provide information on the timing of sequelae. All patients underwent a slit-lamp examination, and as indicated, a dilated fundoscopic examination, such that the prevalence of uveitis is a reliable estimate with minimal selection and measurement bias. This study is also the first to examine the clinical and laboratory predictors of EVD clinical sequelae in convalescence.

Implications of the available evidence

These findings signal an immediate need to systematically provide early clinical follow-up for all survivors of EVD with particular attention paid to the potential for ocular complications. Further research is needed to understand the pathologies underlying the various EVD sequelae.

GOAL Global, International Medical Corps, and Christian Blind Mission under the oversight of the Sierra Leone Ministry of Health and Sanitation (MoHS) District Health Management Team, with technical support from WHO.

Patient population

Survivors of EVD were identified via the MoHS-WHO registry of patients residing in Port Loko District, regardless of where originally treated. All were laboratory confirmed to have EVD through real-time RT-PCR testing on serum and discharged from ETUs after clinical improvement and a negative convalescent real-time RT-PCR. The registry was cross checked against the Sierra Leone Association for Ebola Survivors registry to generate a complete list (appendix). The EVD Survivor Network led community sensitisation regarding the establishment of the clinic. Survivors were systematically contacted by mobile phone by the clinic coordinator according to village of residence. Bus pick-ups were scheduled for each village and patients were assessed in the clinic irrespective of symptoms. We started with villages with resident survivors discharged in the remote past, until all villages were covered. As of Nov 12, 2015, the clinic had assessed 603 survivors of EVD residing in Port Loko at least once.

See Online for appendix

Data collection

We extracted demographic and clinical data from patient charts (appendix) on the first 277 consecutive survivors of EVD assessed in the survivor clinic between March 7, 2015, and April 24, 2015. Eight patients were self-referred with ocular symptoms, but all would nevertheless have been identified through the village selections over the study period. Each patient received a clinical assessment and an eye examination, including visual acuity and slit-lamp examination. Patients with ocular symptoms, decreased visual acuity, or abnormalities on slit-lamp examination also received dilated fundoscopic assessment. Clinical data were entered into an electronic database and linked to two other datasets using the EVD laboratory number, and cross-checked with a unique patient identifier, sex, date of acute EVD testing, and patient residence or age. The additional datasets included: EVD surveillance data, which provided symptoms on presentation; and real-time RT-PCR and cycle threshold (an inversely correlated marker of viral load) results on the subset of patients who were diagnosed or cared for in a Port Loko ETU. The real-time RT-PCR assay used for testing changed after Feb 1, 2015 (appendix). After linkage, anonymised data were used for analyses. The study was approved by the Sierra Leone MoHS and Ethics and Scientific Review Committee.

Data analysis

We used descriptive statistics to report features of acute EVD and clinical symptoms at the first convalescent visit. We used χ^2 or Fisher's exact test for categorical data and the *t* test or Wilcoxon rank-sum test for continuous data to assess the relation between demographics (age, sex), cycle threshold at EVD diagnosis, duration of acute illness (days from symptom onset to the first negative real-time RT-PCR during acute EVD), self-reported symptoms of acute