

Ebola Virus Disease Complications as Experienced by Survivors in Sierra Leone

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Background. Thousands of people have survived Ebola virus disease (EVD) during the ongoing outbreak. However, data about the frequency and risk factors of long-term post-EVD complications remain scarce. We describe the clinical characteristics of EVD survivors followed in a survivor clinic in Freetown, Sierra Leone.

Methods. A survivor clinic opened within an Ebola treatment center compound in Freetown, Sierra Leone. At each visit, clinical and psychological assessments were conducted and free treatment was offered. Survivors were referred to a partner's hospitals if their condition could not be managed in the clinic. We used routinely collected data from the clinic to describe long-term complications of EVD and their risk factors.

Results. A total of 1001 medical consultations for 166 patients were performed between 3 February and 21 June 2015. The most frequent complaints and diagnoses were arthralgia (n = 129 [77.7%]), fatigue (n = 116 [69.8%]), abdominal pain (n = 90 [54.2%]), headache (n = 87 [52.4%]), anemia (n = 83 [50%]), skin disorders (n = 81 [48.8%]), back pain (n = 54 [32.5%]), and alopecia (n = 53 [31.9%]). Ocular complications were diagnosed in 94 survivors (56.7%); uveitis was the most common (n = 57 [34%]). Survivors were 10 times more likely to develop uveitis post-EVD if they presented with red/injected eyes during the acute phase of their illness.

Conclusions. Post-EVD complications among our patients were similar to those described previously and were detected early following the acute phase of disease. Follow-up of survivors should begin immediately after discharge to address sequelae as they arise and reduce the potential for development of long-term disabilities such as blindness.

Keywords. Ebola; survivors; complications.

As of February 2016, >28 000 cases of Ebola virus disease (EVD) have been reported from the epidemic affecting West Africa since December 2013 [1]. The burden of disease was highest in Sierra Leone with >14 000 reported cases. Although many have died, with a case fatality ratio of approximately 50%, thousands have survived the disease [1].

The first report from the Sudan EVD outbreak in 1976 described a “slow and painful” recovery in survivors [2]. Few cohorts have characterized clinical complications [3–14], and only 2 controlled studies have been published [5, 13]. Arthralgia, weakness, hair loss, anorexia, weight loss, abdominal pain, hearing loss and tinnitus, neuropathy, increased susceptibility to infections, and cardiac problems have been reported. Ocular complications, most often uveitis and conjunctivitis, have also

been described in small case series [3–5, 7–9, 11, 14–17]. Whether delayed complications are due to persistent viral replication in immune-protected body sites, immune complex deposition, persistence of virus antigen, molecular mimicry, or another mechanism remains unknown. A better understanding of the long-term physical and psychological complications of EVD is needed to address and prevent long-term sequelae. Here we describe complications among survivors attending an EVD survivor clinic in Freetown, Sierra Leone.

METHODS

Description of the Survivor Clinic

On 10 December 2014, Médecins Sans Frontières (MSF) opened an Ebola treatment center (ETC) in Freetown, Sierra Leone, on the grounds of the Prince of Wales (POW) School. The center admitted any individual with suspected or confirmed EVD. By the time it closed on 25 February 2015, 170 patients with confirmed EVD had been treated and 83 survivors discharged.

On 3 February 2015, an EVD survivor clinic opened on the same compound. All survivors from the POW ETC were invited for follow-up. The clinic was also open for other survivors if their EVD diagnosis was laboratory confirmed. Patients visited the clinic weekly, then bimonthly or monthly before being

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discharged from the program when symptoms receded. For patients in need of care at the time of clinic closure (21 June 2015), continued follow-up was arranged at the eye clinic and/or another survivor clinic.

At each visit, survivors had a consultation with a medical doctor and a session with a mental health counselor, and participated in a support group session led by the health promotion team.

During each medical consultation, history was taken and a complete medical examination performed, including measurement of visual acuity (Supplementary Text 1). Results and subsequent diagnosis were recorded on a standardized medical chart (Supplementary Figure 1).

Patients were treated according to MSF standard protocols [18]. Patients with suspected ocular complications were referred to the Lowell and Ruth Gess UMC Eye Hospital for diagnosis and treatment. Uveitis was treated depending on its localization, with topical and/or oral corticosteroids, mydriatics, and management of intraocular pressure. Patients who needed additional diagnostics or treatment for other conditions were referred to Connaught Hospital in Freetown.

Family planning and counseling on methods to prevent secondary sexual transmission of EVD were offered at each consultation. Survivors were referred to the national human immunodeficiency virus (HIV) program at Connaught Hospital for HIV testing on a voluntary basis.

Survivors had a psychological support session at each visit. Complaints and symptoms were recorded on a standardized questionnaire (Supplementary Figure 2), and psychiatric screening was carried out using the Self Reporting Questionnaire 20 (SRQ-20) [19]. Psychosocial support was provided through individual counseling sessions and intervention of an outreach team in the community when necessary. Support group sessions focused on EVD education, community reintegration, and stigmatization. All medical care and treatment was provided free of charge.

Detailed infection prevention and control procedures are available in Supplementary Text 2.

Data Collection and Statistical Analysis

Anemia was defined as a hemoglobin level <11 g/dL. Visual acuity was coded as “normal vision, mild impairment” if $\geq 6/18$; “moderate impairment” if $<6/18$ and $\geq 6/60$; “severe impairment” if $<6/60$ and $\geq 3/60$; and “blindness” if $<3/60$. Uveitis was classified according to the Standardization of Uveitis Nomenclature [20]. Reverse transcription polymerase chain reaction (RT-PCR) cycle threshold (Ct) values at admission and length of stay in ETC were only available for patients treated in the POW ETC.

After each visit, data were anonymized and entered into an EpiData data mask. Data were stratified and analyzed by age (children ≤ 15 years and adults ≥ 16 years) and time between ETC discharge and first follow-up visit (0–30 days, 31–60

days, 61–90 days, and ≥ 91 days). Patient characteristics were summarized using frequencies and percentages for categorical variables and means and standard deviations (SDs) for continuous variables. Comparisons between demographic characteristics and the occurrence of symptoms were made using χ^2 or Fisher exact test for categorical variables and *t* test or analysis of variance for continuous variables. Results are presented with their 95% confidence intervals (CIs) where appropriate.

Univariate and multivariable logistic regression models were fitted to explore the risk factors for being diagnosed with uveitis, having any ocular complication, and arthralgia. Age, sex, Ct value at ETC admission, ETC of discharge, days hospitalized in the ETC, time from ETC discharge to first follow-up visit, and having had a red/injected eye while hospitalized in the ETC were included as potential confounders in the analysis. The cutoff for the continuous variable, days hospitalized in the ETC, was defined based on its median value.

Patients with complete data on variables of interest were retained for multivariable analysis. Adjusted odds ratios (aORs) and their 95% CIs were calculated. Statistical analysis was performed using Stata 12 software (StataCorp, College Station, Texas).

The analysis was based on routinely collected program data from a survivor clinic; ethical review and individual patient consent were not sought. Data used for analysis were anonymized.

RESULTS

A total of 166 survivors were followed between 3 February and 21 June 2015. Among the 83 EVD survivors from POW ETC, 81 were followed up; 2 died before the program started. The 85 others were relatives of POW ETC survivors or had been treated in other ETCs.

Characteristics of survivors are summarized in Table 1. More than half were male, with a mean age of 24.7 years. Survivors had an average of 4.3 follow-up visits. Mean Ct value at ETC admission was 22.1 and mean length of hospitalization was 11.1 days.

Table 2 summarizes the prevalence of complications among children and adult EVD survivors. The most common complication was arthralgia (78%), which was predominately polyarticular and symmetrical and reported to be more intense in the morning and to increase after exercise. Redness or functional limitations were not detected. Only 1 survivor presented with a monoarticular proximal interphalangeal joint effusion of the left hand without previous history of trauma or rheumatic disease. The radiograph showed no abnormalities. The swelling lasted 3 weeks and resolved with empiric antibiotic treatment.

As seen in Table 2, survivors also complained of fatigue (69.8%), abdominal pain (54.2%), and headache (52.4%). Half were diagnosed with anemia and 48.8% had skin manifestations (impetigo, scabies, desquamation, or generalized pruritus).

Table 1. Characteristics of Ebola Virus Disease Survivors Enrolled in the Médecins Sans Frontières Follow-up Program in Freetown, Sierra Leone

Characteristic	All (N = 166)	Adults (≥16 y) (n = 128)	Children (≤15 y) (n = 38)
Visit frequency and time			
Total visits, No. (range)	1001 (1–13)	748 (1–13)	253 (1–13)
Days between ETC discharge and first follow-up, mean (SD)	51.1 (41.2)	53.8 (42.3)	42.0 (36.3)
Days of follow-up in MSF survivor clinic, mean (SD)	55.8 (30.8)	54.7 (30.4)	59.7 (32.5)
First follow-up within 14 d of ETC discharge, No. (%)	35 (21.0)	25 (19.5)	10 (26.3)
Baseline characteristics			
Age category, No. (%)			
0–59 m	10 (6.0)		10 (22.2)
5–15 y	28 (16.8)		28 (73.7)
16–30 y	83 (50)	83 (64.8)	
≥30 y	45 (27.1)	45 (35.1)	
Age, y, mean (SD)	24.7 (12.7)	29.4 (10.5)	9.1 (4.1)
Sex			
Male	92 (55.4)	63 (49.2)	29 (76.3)
Female	74 (44.5)	65 (50.7)	9 (23.7)
Ct value at admission, mean (SD) ^a	22.1 (4.03)	22.2 (4.0)	22.1 (4.5)
Days hospitalized in the ETC, mean (SD) ^a	11.1 (5.7)	10.5 (5.0)	12.6 (7.0)

Abbreviations: Ct, cycle threshold; ETC, Ebola treatment center; MSF, Médecins Sans Frontières; SD, standard deviation.

^a Survivors from MSF Prince of Wales only: n = 77 (adults, n = 55; children, n = 22).

Other infectious syndromes were also common. Of the 75 survivors who shared their HIV result, all tested negative.

Several survivors had evidence of cardiovascular disease (valvulopathy, 5; tachycardia, 2; hypertensive cardiopathy, 1; cardiac decompensation, 1); one had suspected deep vein thrombosis. Two male survivors in their twenties, without known history of heart disease, presented with chest pain, dyspnea on exertion, and palpitations without sign of heart failure. They were referred to Connaught Hospital for assessment by a cardiologist after their electrocardiograms showed signs of myocarditis. The result of the transthoracic echography was compatible with myocarditis in one boy whereas no abnormalities were found in the second. Seven women reported amenorrhea. All but one, who became pregnant during the follow-up period and delivered a healthy baby after the closure of the clinic, had a negative pregnancy test (Supplementary Text 2).

Ninety-seven EVD survivors with suspected ocular complications were referred to the eye clinic. Twenty of the 94 (22%) patients with identified ophthalmological abnormalities were children (Table 2). Overall, the most common diagnosis was uveitis (n = 58 [61.7%]), particularly in survivors 16–30 years of age (Supplementary Table 1), followed by conjunctivitis or allergic conjunctivitis, cataract, and glaucoma (Supplementary Table 2). Uveitis was predominantly bilateral (n = 32 [59%]),

Table 2. Prevalence of Signs, Symptoms, and Diagnoses in Ebola Virus Disease Survivors Enrolled in the Médecins Sans Frontières Follow-up Program in Freetown, Sierra Leone

Signs, Symptoms, and Diagnoses	All (N = 166)	Adults (≥16 y) (n = 128)	Children (≤15 y) (n = 38)	P Value
Arthralgia	129 (77.7)	109 (85.1)	20 (52.6)	≤.001
Fatigue	116 (69.8)	94 (73.4)	22 (57.8)	.067
Abdominal pain	90 (54.2)	72 (56.2)	18 (47.3)	.335
Headache	87 (52.4)	66 (51.5)	21 (55.3)	.688
Anemia	83 (50)	55 (42.9)	28 (73.7)	.001
Skin rash or infection/itching/desquamation	81 (48.8)	54 (41.2)	27 (71.0)	.002
Back pain	54 (32.5)	46 (35.9)	8 (21.0)	.085
Alopecia (diffuse)	53 (31.9)	43 (33.5)	10 (26.3)	.398
Respiratory tract infection + otitis	45 (27.1)	29 (22.6)	16 (42.1)	.018
Anorexia	43 (25.9)	36 (28.1)	7 (18.4)	.294
Genital/urinary tract infection/STI	38 (22.8)	36 (28.1)	2 (5.3)	.002
Insomnia	30 (18.0)	29 (22.6)	1 (2.6)	.003
Gastritis/ulcer/GERD	27 (16.2)	26 (20.3)	1 (2.6)	.01
Malaria	23 (13.8)	14 (10.9)	9 (23.7)	.046
Moderate acute malnutrition	19 (11.4)	7 (5.4)	12 (31.6)	≤.001
Cardiopathy/valvulopathy/tachycardia	19 (11.4)	17 (13.2)	2 (5.3)	.248
Amenorrhea ^a	7 (10.1)	7 (10.7)	0	.353
Arterial hypertension	12 (7.2)	12 (9.3)	0	.07
Diarrhea/gastroenteritis	9 (5.4)	7 (5.4)	2 (5.3)	1
Tinnitus/hearing loss	5 (3.0)	4 (3.1)	1 (2.6)	1
Severe acute malnutrition	2 (1.2)	0	2 (5.3)	.051
Myocarditis (clinically suspect)	2 (1.2)	2 (1.5)	0	1
Any ocular complication	94 (56.6)	74 (57.8)	20 (52.6)	.61
Uveitis	58 (34.9)	50 (39.0)	8 (32.1)	.03

Data are presented as No. (%).

Abbreviations: GERD, gastroesophageal reflux disease; STI, sexually transmitted infection.

^a Considered only for women >10 years of age: n = 69 for all (n = 65 for adults, n = 4 for children aged 10–15 years).

anterior (n = 36 [62%]), or panuveitis (n = 13 [21%]). In 57 patients, uveitis was diagnosed at the first visit to the eye clinic, including a survivor who had been discharged from the ETC the previous week. Seven patients with uveitis were also diagnosed with cataract; in at least 3 of these patients the cataract developed after diagnosis of uveitis. Visual acuity did not change during the follow-up period in the majority of uveitis patients; however, it worsened unilaterally in 4 patients and improved in 9. None of the patients who were followed up and treated within 30 days after ETC discharge had visual acuity that deteriorated further.

Most (77%) survivors had their first follow-up within 3 months after discharge from the ETC. Complications were more frequently reported by survivors who had their first

Table 3. Prevalence of Signs, Symptoms, and Diagnoses in Ebola Virus Disease Survivors Enrolled in the Médecins Sans Frontières Follow-up Program, by Days Between Ebola Treatment Center Discharge and First Follow-up Visit, Freetown, Sierra Leone

Signs, Symptoms, and Diagnoses	Overall (N = 166)	Days From ETC Discharge to First Follow-up Visit				P Value
		0–30 d (n = 62)	31–60 d (n = 45)	61–90 d (n = 21)	≥91 d (n = 38)	
Arthralgia	129 (77.7)	48 (77.4)	34 (75.5)	18 (85.7)	29 (76.3)	.815
Fatigue	116 (69.8)	51 (82.3)	22 (48.9)	16 (76.1)	27 (71.0)	.002
Abdominal pain	90 (54.2)	40 (64.5)	21 (51.1)	14 (66.7)	12 (34.2)	.016
Headache	87 (52.4)	36 (58.0)	25 (55.6)	11 (52.4)	15 (39.5)	.318
Anemia	83 (50.0)	36 (58.0)	22 (48.8)	11 (52.3)	14 (36.8)	.229
Skin rash or infection/itching/desquamation	81 (48.8)	38 (61.2)	21 (46.7)	9 (42.8)	13 (34.2)	.058
Back pain	54 (32.5)	25 (40.3)	14 (31.1)	8 (38.1)	7 (18.4)	.139
Alopecia (diffuse)	53 (31.9)	23 (37.1)	8 (17.8)	10 (47.6)	12 (31.6)	.063
Respiratory tract infection + otitis	45 (27.1)	17 (27.4)	18 (40.0)	3 (14.3)	7 (18.4)	.072
Anorexia	43 (25.9)	21 (33.8)	11 (24.4)	5 (23.8)	6 (15.8)	.243
Genital/urinary tract infection/STI	38 (22.8)	22 (35.5)	5 (11.1)	3 (14.3)	8 (21.0)	.018
Insomnia	30 (18.0)	10 (16.1)	7 (15.6)	4 (19.0)	9 (23.7)	.760
Gastritis/ulcer/GERD	27 (16.2)	11 (17.7)	7 (15.5)	4 (19.0)	5 (13.2)	.918
Malaria	23 (13.8)	10 (16.1)	3 (6.7)	2 (9.5)	8 (21.0)	.241
Moderate acute malnutrition	19 (11.4)	10 (16.1)	6 (13.3)	1 (4.7)	2 (5.2)	.277
Cardiopathy/valvulopathy/tachycardia	19 (11.4)	7 (11.3)	6 (13.3)	2 (9.5)	4 (10.5)	.966
Amenorrhea ^a	7 (10.1)	0 (0.0)	3 (16.7)	0 (0.0)	4 (26.7)	.045
Arterial hypertension	12 (7.2)	4 (6.4)	4 (8.8)	1 (4.7)	3 (7.8)	.928
Diarrhea/gastroenteritis	9 (5.4)	5 (8.0)	2 (4.4)	0 (0.0)	2 (5.3)	.545
Tinnitus/hearing loss	5 (3.0)	1 (1.6)	3 (6.7)	0 (0.0)	1 (2.6)	.370
Severe acute malnutrition	2 (1.2)	1 (1.6)	1 (2.2)	0 (0.0)	0 (0.0)	.754
Myocarditis (clinically suspect)	2 (1.2)	1 (1.6)	1 (2.2)	0 (0.0)	0 (0.0)	.754
Any ocular complication	94 (56.6)	41 (66.1)	22 (48.8)	11 (52.3)	20 (52.6)	.353
Uveitis	58 (34.9)	26 (41.9)	10 (22.2)	8 (38.0)	14 (36.8)	.213

Data are presented as No. (%).

Abbreviations: ETC, Ebola treatment center; GERD, gastroesophageal reflux disease; STI, sexually transmitted infection.

^a Considered only for women >10 years of age: n = 69 for all (n = 26 for 0–30 days, n = 18 for 31–60 days, n = 10 for 61–90 days, n = 15 for ≥91 days).

follow-up visit within 3 months of discharge (Table 3). Most of the complications were detected at the first visit (Supplementary Table 3); alopecia and malaria were more frequently reported by survivors after ≥60 days had passed between discharge from the ETC and their first follow-up visit (Supplementary Table 4). The number of follow-up visits per complaint can be found in Supplementary Table 5.

Table 4 shows risk factors for developing uveitis, any ocular symptom, or arthralgia. The main risk factor for developing uveitis in adjusted analysis was having had red/injected eye during ETC hospitalization (aOR, 10.3 [95% CI, 2.02–53.3]), whereas younger age appeared protective (aOR, 0.12 [95% CI, .02–.74]). We found no association between uveitis and markers of disease severity (Ct value at admission or duration of hospitalization). Having any ocular complication was not associated with any of the risk factors in our analysis. For arthralgia, young age appeared protective.

At their first visit with the psychological support team, several survivors described stigma: 27% (31/145) reported feeling ashamed or embarrassed by their status and 26% (29/113) reported being avoided by others. Eighteen percent (30/166)

reported insomnia. Hallucinations were described by 5 survivors and irritable mood by 4. The median score for emotional distress as assessed by the SRQ-20 was 4.

DISCUSSION

Similar to historic descriptions, the most common post-EVD complications in our cohort were arthralgia, fatigue, and ocular complications. Two recent articles from Sierra Leone describe similar complications. In a cross-sectional study of survivors from Port Loko (median 121 days post-ETC discharge), Mattia et al reported arthralgia, ocular complications, and auditory symptoms as occurring frequently in their cohort [9], while Scott et al described musculoskeletal pain, headache, and ocular symptoms in the first visit 2–3 weeks post-ETC discharge [3]. In contrast to Mattia et al's report, few survivors in our cohort experienced auditory symptoms; however, such complications may occur later in the post-EVD period. Nevertheless, no difference was shown between survivors and controls in the only controlled study employing audiometric testing [13].

Arthralgia and back pain have been described in up to 88% of survivors during the 2013–2015 EVD outbreak [12] and can

Table 4. Univariate and Multivariable Analyses: Risk Factors for Sequelae of Acute Ebola Virus Disease Among Survivors Enrolled in the Médecins Sans Frontières Follow-up Program, Freetown, Sierra Leone

Risk Factor	Uveitis		Any Ocular Complication		Arthralgia	
	OR (95% CI) (N = 166)	Adjusted ^a OR (95% CI) (n = 65)	OR (95% CI) (N = 166)	Adjusted ^a OR (95% CI) (n = 65)	OR (95% CI) (N = 166)	Adjusted ^a OR (95% CI) (n = 65)
Age, y						
0–15	0.40 (.16–.98) ^b	0.16 (.02–1.17)	0.81 (.37–1.75)	0.90 (.23–3.47)	0.18 (.07–.45) ^b	0.08 (.016–.41) ^b
16–30	1	1	1	1	1	1
≥31	0.91 (.43–1.93)	2.39 (.40–14.16)	0.99 (.47–2.08)	2.22 (.44–11.14)	0.91 (.33–2.52)	0.61 (.08–4.47)
Sex						
Male	1	1	1	1	1	1
Female	1.55 (.81–2.96)	4.38 (.87–22.0)	1.36 (.73–2.53)	1.93 (.58–6.46)	1.42 (.67–3.02)	0.35 (.71–1.80)
ETC of discharge						
MSF Prince of Wales	1	...	1	...	1	...
Other	0.96 (.51–1.83)	...	1.11 (.60–2.06)	...	0.76 (.36–1.58)	...
Time to first follow-up						
0–30 d	1	1	1	1	1	1
31–60 d	0.39 (.16–.93) ^b	0.18 (.04–.84) ^b	0.48 (.22–1.07)	0.49 (.16–1.45)	0.90 (.36–2.22)	1.45 (.34–6.15)
61–90 d	0.85 (.30–2.35)	...	0.56 (.20–1.53)	...	1.75 (.44–6.81)	...
≥90 d	0.80 (.35–1.85)	...	0.56 (.24–1.29)	...	0.93 (.36–2.44)	...
Joint pain during follow-up						
No	1	1	1	1	1	1
Yes	1.15 (.53–2.51)	1.90 (.34–10.63)	0.99 (.47–2.07)	1.07 (.28–4.05)	1.15 (.53–2.51)	2.33 (.38–14.1)
Ct value ^c	0.95 (.84–1.07)	0.99 (.82–1.21)	1.02 (.91–1.15)	1.05 (.92–1.21)	0.99 (.87–1.13)	1.04 (.88–1.24)
Days hospitalized^c						
1–10	1	1	1	1	1	1
≥11	1.10 (.45–2.83)	0.37 (.08–1.64)	0.83 (.34–2.02)	0.72 (.22–2.32)	0.97 (.35–2.67)	1.88 (.45–7.75)
Red/injected eye in ETC^c						
No	1	1	1	1	1	1
Yes	3.34 (1.18–9.45) ^b	10.4 (1.91–57.5) ^b	2.22 (.77–6.38)	2.84 (.81–9.86)	2.18 (.63–7.58)	1.53 (.30–7.61)

Abbreviations: CI, confidence interval; Ct, cycle threshold; ETC, Ebola treatment center; MSF, Médecins Sans Frontières; OR, odds ratio.

^a In final adjusted model, analysis is restricted to those patients for whom all data were available.

^b Confidence intervals that do not overlap the null values of OR = 1, $P \leq .05$.

^c Only survivors from MSF Prince of Wales; Ct value, $n = 77$; days hospitalized, $n = 81$; red/injected eye in ETC, $n = 70$.

hinder their ability to work [14], thus increasing the burden of the disease by its impact on household income. Joint effusion was rare in our and other cohorts [3, 9, 13, 14].

In our cohort, 57% of survivors developed ocular complications; uveitis was the most commonly diagnosed as previously reported [4, 7–9, 11, 15–17], and was mostly present at the first visit. In at least 1 survivor treated in the United States, uveitis was diagnosed during the acute phase of EVD [16]. In our cohort, patients with red/injected eyes during ETC hospitalization were 10 times more likely to develop uveitis. Redness of the eye at presentation could indicate that the conjunctiva is the primary site of infection. Whether it facilitates viral spread to deeper compartments of the eye, generating a higher viral load inside those different fluid compartments and potentially leading to delayed viral clearance and uveitis, remains unclear. Others identified more severe disease (low Ct value) being a strong risk factor for developing uveitis or eye complications [9]. This would be consistent with the hypothesis that severe, prolonged disease leads to persistence of virus [17]. We were not

able to confirm this in our cohort, but the number of patients with Ct values available was small.

Screening for eye symptoms should begin during hospitalization, and treatment should be initiated as soon as possible. Treatment of uveitis is simple and inexpensive but requires specific material such as slit lamps and special training to identify disease and other medical conditions that could contraindicate the use of steroids. The fact that Ebola virus was isolated from the aqueous humor of a survivor treated in the United States who presented with panuveitis 14 weeks after EVD onset [17] may further complicate treatment. In at least 3 of our patients, cataracts developed as a complication of uveitis. Although sight may be improved by cataract surgery, the presence of potentially infectious virus in the anterior segment would make such a procedure dangerous.

A number of patients presented with symptoms of cardiovascular disease. Euthyroid sick syndrome has been diagnosed in a survivor treated in Europe [21]. The implication of thyroid dysfunction in survivors presenting with tachycardia remains to be determined. Evidence of mild focal myocarditis has been

described postmortem at autopsy [2], and pericarditis was clinically suspected after the 1995 Kikwit epidemic [4].

EVD survivors are confronted with stigmatization upon returning to their communities [6, 10, 22–25]. In Lagos, Nigeria, 62% and 64% of study respondents reported being unwilling to shake hands with or hug a survivor [23]. After the 1995 Kikwit outbreak, up to 35% of survivors reported being rejected by family, friends, or neighbors [6]. Alopecia, especially in women, is a visible complication of EVD and could increase discrimination. Our patients often reported being subjected to intense stigmatization, even within their households. Many expressed being sad due to the loss of family members and witnessing deaths, and feared the future. The median score of psychological distress measured by the SRQ-20, never validated in the Sierra Leonean population, could underestimate the prevalence of distress in the survivors, as they showed sustained expressions of sadness, grief, and regular bursts of crying during the consultations. The cutoff for psychiatric disturbance is unknown and requires further assessment. The role of emotional distress in the persistence of symptoms remains to be established.

All survivors from POW ETC who were alive responded to the invitation and came for follow-up. However, 2 died after being discharged from the ETC with a negative RT-PCR test, before the clinic was opened. Further information was available for one who died 26 days after discharge and reported dyspnea and swelling of one leg prior to death. The clinical picture could be a complication of acute disease, perhaps a pulmonary embolism following deep vein thrombosis; the postmortem oral swab tested positive for Ebola virus by RT-PCR. Whether detectable virus was a consequence of virus shedding after the acute phase or reactivation remains unknown.

This descriptive analysis has several limitations. The data were not collected systematically and data are missing even after using standardized forms. Our cohort was small and some observations may be due to chance; however, the majority of our findings are in line with previous descriptions. The risk factor analysis for uveitis was limited by the small subgroup of patients for whom complete data were available. There was no control group, so we cannot judge how these findings compare to the general population. We followed patients soon after discharge but only for a few months; some complications may have arisen later. A description of larger cohorts over an extended period of time with better diagnostic means is needed to fully determine the extent of complications.

CONCLUSIONS

Our results confirm previous descriptions of the burden of post-EVD complications. We showed that the majority of complications start soon after discharge and suggest that care for survivors should begin during hospitalization and immediately after discharge to detect and treat complications early, with the aim of preventing long-term disability. While there is evidence

of virus persistence in a few immunologically protected body sites (semen [26, 27], anterior chamber of the eye [17], and central nervous system [28]), its role in post-EVD complications remains unknown. A better understanding of pathophysiology is needed to propose the best treatment strategy and explore the role of antiviral therapy during the post-EVD phase. For future outbreaks, survivor care, including psychological and ophthalmic care, should begin early and be standard practice.

Supplementary Data

Supplementary materials are available at <http://cid.oxfordjournals.org>. Consisting of data provided by the author to benefit the reader, the posted materials are not copyrighted and are the sole responsibility of the author, so questions or comments should be addressed to the author.

Notes

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References

1. World Health Organization. Ebola response roadmap situation report. Available at: <http://apps.who.int/ebola/current-situation/ebola-situation-report-2-march-2016>. Accessed 6 March 2016.
2. World Health Organization. Ebola haemorrhagic fever in Sudan, 1976. Report of a WHO/International Study Team. *Bull World Health Organ* **1978**; 56:247–70.
3. Scott JT, Sesay FR, Massaquoi TA, Idriss BR, Sahr F, Semple MG. Post-Ebola syndrome, Sierra Leone. *Emerg Infect Dis* **2016**; 22:641–6.
4. Bwaka MA, Bonnet MJ, Calain P, et al. Ebola hemorrhagic fever in Kikwit, Democratic Republic of the Congo: clinical observations in 103 patients. *J Infect Dis* **1999**; 179(suppl 1):S1–7.
5. Clark DV, Kibuuka H, Millard M, et al. Long-term sequelae after Ebola virus disease in Bundibugyo, Uganda: a retrospective cohort study. *Lancet Infect Dis* **2015**; 15:905–12.
6. De Roo A, Ado B, Rose B, Guimard Y, Fonck K, Colebunders R. Survey among survivors of the 1995 Ebola epidemic in Kikwit, Democratic Republic of Congo: their feelings and experiences. *Trop Med Int Health* **1998**; 3:883–5.
7. Epstein L, Wong KK, Kallen AJ, Uyeki TM. Post-Ebola signs and symptoms in U.S. survivors. *N Engl J Med* **2015**; 373:2484–6.
8. Kibadi K, Mupapa K, Kuvula K, et al. Late ophthalmologic manifestations in survivors of the 1995 Ebola virus epidemic in Kikwit, Democratic Republic of the Congo. *J Infect Dis* **1999**; 179(suppl 1):S13–4.
9. Mattia JG, Vandy MJ, Chang JC, et al. Early clinical sequelae of Ebola virus disease in Sierra Leone: a cross-sectional study. *Lancet Infect Dis* **2016**; 16:331–8.
10. Mohammed A, Sheikh TL, Gidado S, et al. An evaluation of psychological distress and social support of survivors and contacts of Ebola virus disease infection and their relatives in Lagos, Nigeria: a cross sectional study—2014. *BMC Public Health* **2015**; 15:824.
11. Nanyonga MSJ, Ramsay A, Shindo N, Bausch DG. Sequelae of Ebola virus disease, Kenema District, Sierra Leone. *Clin Infect Dis* **2016**; 62:125–6.
12. Qureshi AI, Chughtai M, Loua TO, et al. Ebola virus disease survivors study in Guinea. *Clin Infect Dis* **2015**; 61:1035–42.

13. Rowe AK, Bertolli J, Khan AS, et al. Clinical, virologic, and immunologic follow-up of convalescent Ebola hemorrhagic fever patients and their household contacts, Kikwit, Democratic Republic of the Congo. *commission de Lutte contre les Epidemies a Kikwit. J Infect Dis* **1999**; 179(suppl 1):S28–35.
14. Wendo C. Caring for the survivors of Uganda's Ebola epidemic one year on. *Lancet* **2001**; 358:1350.
15. Chancellor JR, Padmanabhan SP, Greenough TC, et al. Uveitis and systemic inflammatory markers in convalescent phase of Ebola virus disease. *Emerg Infect Dis* **2016**; 22:295–7.
16. Jampol LM, Ferris FL 3rd, Bishop RJ. Ebola and the eye. *JAMA Ophthalmol* **2015**; 133:1105–6.
17. Varkey JB, Shantha JG, Crozier I, et al. Persistence of Ebola virus in ocular fluid during convalescence. *N Engl J Med* **2015**; 372:2423–7.
18. I Broek NH, Henkens M, Mekaoui H, Palma P, Szumilin E, Grouzard V. *Clinical guidelines diagnostic and treatment manual. 2013 rev. ed. Geneva, Switzerland: Médecins Sans Frontières, 2013.*
19. World Health Organization. A User's guide to the self reporting questionnaire. Available at: http://apps.who.int/iris/bitstream/10665/61113/1/WHO_MNH_PSF_94.8.pdf. Accessed 4 September 2015.
20. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. *Am J Ophthalmol* **2005**; 140:509–16.
21. Mora-Rillo M, Arsuaga M, Ramirez-Olivencia G, et al. Acute respiratory distress syndrome after convalescent plasma use: treatment of a patient with Ebola virus disease contracted in Madrid, Spain. *Lancet Respir Med* **2015**; 3:554–62.
22. Hugo M, Declerck H, Fitzpatrick G, et al. Post-traumatic stress reactions in Ebola virus disease survivors in Sierra Leone. *Emerg Med (Los Angel)* **2015**; 5:1–4.
23. Gidado S, Oladimeji AM, Roberts AA, et al. Public knowledge, perception and source of information on Ebola virus disease—Lagos, Nigeria; September, 2014. *PLoS Curr* **2015**; 7.
24. Hewlett BS, Amola RP. Cultural contexts of Ebola in northern Uganda. *Emerg Infect Dis* **2003**; 9:1242–8.
25. Arwady MA, Garcia EL, Wollor B, et al. Reintegration of Ebola survivors into their communities—Firestone District, Liberia, 2014. *MMWR Morb Mortal Wkly Rep* **2014**; 63:1207–9.
26. Deen GF, Knust B, Broutet N, et al. Ebola RNA persistence in semen of Ebola virus disease survivors—preliminary report. *N Engl J Med* **2015**; doi:10.1056/NEJMoa1511410.
27. Rodriguez LL, De Roo A, Guimard Y, et al. Persistence and genetic stability of Ebola virus during the outbreak in Kikwit, Democratic Republic of the Congo, 1995. *J Infect Dis* **1999**; 179(suppl 1):S170–6.
28. O'Carroll L. Ebola nurse Pauline Cafferkey nearly died from meningitis, doctors say. Available at: <http://www.theguardian.com/world/2015/oct/21/ebola-nurse-pauline-cafferkey-condition-serious-but-stable-royal-free-hospital>. Accessed 27 October 2015.