Ebola Virus Disease Complications as Experienced by Survivors in Sierra Leone.

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40 words summary: The main complications experienced by survivors in our clinic were arthralgia and uveitis as described earlier. Treatment of EVD complications should be systematic and initiated as soon as possible to prevent severe disabilities such as blindness.

Abstract

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 and Conclusions: 1001 medical consultations for 166 patients were carried out between 3 February and 21 June 2015. The most frequent complaints and diagnoses were arthralgia (77.7%, n=129), fatigue (69.8%, n=116), abdominal pain (54.2%, n=90) headache (52.4%, n=87), anemia (50%, n=83) skin disorders (48.8%, n=81), back pain (32.5%, n=54), and alopecia (n=53, 31.9%). Ocular complications were diagnosed in 94 survivors (56.7%); uveitis was the most common (34%, n=57). 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. Post-EVD complications among our patients were similar to those described previously and were detected early following acute phase of disease. Follow-up of survivors should begin immediately after discharge in order to address sequelae as they arise and reduce the potential for development of long-term disabilities such as blindness.

Background

As of February 2016, over 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 over 14,000 reported cases. While 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/or 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 December 10, 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 February 25, 2015, 170 patients with confirmed EVD had been treated and 83 survivors discharged.

On February 3, 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 bi-monthly or monthly

before being discharged from the program when symptoms receded. For patients in need of care at the time of clinic closure (June 21, 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, a session with a mental health counselor and participated in a support group session lead by the health promotion team.

During each medical consultation history was taken and a complete medical examination performed including measurement of visual acuity (see Supplementary Text S1). Results and subsequent diagnosis were recorded on a standardized medical chart (see Supplementary Figure S1).

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 intra-ocular 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 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 (see Supplementary Figure S2) and psychiatric screening was carried out using the Self Reporting Questionnaire 20 (SRQ20) [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 S2.

Data collection and statistical analysis

Anemia was defined as a hemoglobin level less than 11g/dl. Visual acuity was coded as "normal vision, mild impairment" if ≥6/18; "moderate impairment" if < 6/18 and ≥6/60; "severe impairment" if less than <6/60 and ≥3/60 and "blindness" if <3/60. Uveitis was classified according to the Standardization of Uveitis Nomenclature (SUN) [20]. Reverse-transcriptase polymerase chain reaction (RT-PCR) cycle threshold (CT) values at admission and length of stay in ETC were only available for patients treated in 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 (SD) for continuous variables. Comparisons between demographic characteristics and the occurrence of symptoms were made using chi-square or Fisher's exact test for categorical and t-test or analysis of variance (ANOVA) for continuous variables. Results are presented with their 95% confidence intervals (95% CI) 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 (aOR) and their 95% CI were calculated. Statistical analysis was performed using Stata 12 software (Stata Corporation, College Station, TX, USA).

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

Survivor's characteristics are summarized in Table 1. Over 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 one survivor presented with a monoarticular proximal interphalangeal joint effusion of the left hand without previous history of trauma or rheumatic disease. The X-ray showed no abnormalities. The swelling lasted 3 weeks and resolved with empirical 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 anaemia and 48.8% had skin manifestations (impetigo, scabies, desquamation, or generalized pruritus). 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 EKGs showed signs of myocarditis. The result of the transthoracic echography was compatible with myocarditis in one boy while 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 (see Supplementary Text S2).

Ninety-seven EVD survivors with suspected ocular complications were referred to the eye clinic. Twenty (22%) of the 94 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 (see Supplementary Table S1) followed by conjunctivitis or allergic conjunctivitis, cataract and glaucoma (see Supplementary Table S2). Uveitis was predominantly bilateral (n=32, 59%), 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 follow-up visit within 3 months of discharge (Table 3). Most of the complications were detected at the first visit (see Supplementary Table S3), alopecia and malaria were more frequently reported by survivors after 60 or more days had passed between discharge from the ETC and their first follow-up visit (see Supplementary Table S4). The number of follow-up visits per complaint can be found in Supplementary Table S5.

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) while younger age appeared protective (aOR 0.12;

95%CI, 0.02-0.74). 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) 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 papers 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 first visit 2-3 weeks post-ETC discharge [3]. In contrast to *Mattia*, few survivors in our cohort experienced auditory symptoms however such complications may occur later in 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 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 one survivor treated in the US, uveitis was diagnosed during the acute phase of EVD [16]. In our cohort, patients with red/injected eyes during ETC hospitalization were ten 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, which could lead to delayed viral clearance and uveitis remains unclear. Others identified more severe disease (low CT value) being 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 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 EBOV was isolated from the aqueous humor of a survivor treated in the US 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. While 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 post-mortem at autopsy [2] and pericarditis was clinically suspected after the 1995 Kikwit epidemic [4].

EVD survivors are confronted with stigmatization once 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

SRQ20, 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 burst of crying during the consultations. The cut-off 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 post-mortem oral swab tested positive for EBOV 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 was 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 in order 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 in

central nervous system [28]), its role in post-EVD complications remains unknown. A better understanding of pathophysiology is needed in order to propose the best treatment strategy and explore the role of antiviral therapy during post-EVD phase. For future outbreaks, survivor care, including psychological and ophthalmic care should begin early and be standard practice.

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Conflict of interest:

The authors report no conflict of interest.

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Table 1: Characteristics of EVD survivors enrolled in the MSF follow-up program in Freetown, Sierra Leone.

Characteristics	All N=166	Adults (≥16 years) N=128	Children (0-15 years) N=38
Visit frequency and time			
Total visits, N (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 days of ETC discharge, n (%)	35 (21.0)	25 (19.5)	10 (26.3)
Baseline characteristics			
Age categories, n (%)			
0-5 years	10 (6.0)		10 (22.2)
5-15 years	28 (16.8)		28 (73.7)
15-30 years	83 (50)	83 (64.8)	
30+ years	45 (27.1)	45 (35.1)	
Age, mean (SD)	24.7 (12.7)	29.4 (10.5)	9.1 (4.1)
Gender			
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: SD, standard deviation.

[a]Survivors from MSF Prince of Wales only, N=77; Adults, n=55; Children n=22.

Table 2: Prevalence of signs, symptoms and diagnoses in EVD survivors enrolled in the MSF follow-up program in Freetown, Sierra Leone.

Signs, symptoms and diagnoses	All N=166 n (%)	Adults (≥16 years) N=128 n (%)	Children (0-15 years) N=38 n (%)	p-value
Arthralgia	129 (77.7)	109 (85.1)	20 (52.6)	≤0.001
Fatigue	116 (69.8)	94 (73.4)	22 (57.8)	0.067
Abdominal Pain	90 (54.2)	72 (56.2)	18 (47.3)	0.335
Headache	87 (52.4)	66 (51.5)	21 (55.3)	0.688
Anemia	83 (50)	55 (42.9)	28 (73.7)	0.001
Skin rash or infection/Itching/Desquamation	81 (48.8)	54 (41.2)	27 (71.0)	0.002
Back pain	54 (32.5)	46 (35.9)	8 (21.0)	0.085
Alopecia (diffuse)	53 (31.9)	43 (33.5)	10 (26.3)	0.398
Respiratory tract infection + Otitis	45 (27.1)	29 (22.6)	16 (42.1)	0.018
Anorexia	43 (25.9)	36 (28.1)	7 (18.4)	0.294
Genital/Urinary tract infection/STI	38 (22.8)	36 (28.1)	2 (5.3)	0.002
Insomnia	30 (18.0)	29 (22.6)	1 (2.6)	0.003
Gastritis/Ulcer/Gastroesophageal reflux disease	27 (16.2)	26 (20.3)	1 (2.6)	0.01
Malaria	23 (13.8)	14 (10.9)	9 (23.7)	0.046
Moderate acute malnutrition	19 (11.4)	7 (5.4)	12 (31.6)	≤0.001
Cardiopathy/Valvulopathy/Tachycardia	19 (11.4)	17 (13.2)	2 (5.3)	0.248
Amenorrhea[a]	7 (10.1)	7 (10.7)	0	0.353
Arterial hypertension	12 (7.2)	12 (9.3)	0	0.07
Diarrhea/Gastroenteritis	9 (5.4)	7 (5.4)	2 (5.3)	1
Tinitus/Hearing loss	5 (3.0)	4 (3.1)	1 (2.6)	1
Severe acute malnutrition	2 (1.2)	0	2 (5.3)	0.051
Myocarditis (clinically suspect)	2 (1.2)	2 (1.5)	0	1
Any ocular complication	94 (56.6)	74 (57.8)	20 (52.6)	0.61
Uveitis	58 (34.9)	50 (39.0)	8 (32.1)	0.03

Abbreviations: 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 between 10 and 15.

Table 3 : Prevalence of signs, symptoms and diagnoses in EVD survivors enrolled in the MSF follow-up program by days between ETC discharge and first follow-up visit, Freetown, Sierra Leone.

Signs, symptoms and diagnoses	Overall N=166 n (%)	Days from ETC discharge to first follow-up visit				
		0-30 days N=62 n (%)	31-60 days N=45 n (%)	61-90 days N=21 n (%)	≥91 days N=38 n (%)	p-value
Arthralgia	129 (77.7)	48 (77.4)	34 (75.5)	18 (85.7)	29 (76.3)	0.815
Fatigue	116 (69.8)	51 (82.3)	22 (48.9)	16 (76.1)	27 (71.0)	0.002
Abdominal Pain	90 (54.2)	40 (64.5)	21 (51.1)	14 (66.7)	12 (34.2)	0.016
Headache	87 (52.4)	36 (58.0)	25 (55.6)	11 (52.4)	15 (39.5)	0.318
Anemia	83 (50.0)	36 (58.0)	22 (48.8)	11 (52.3)	14 (36.8)	0.229
Skin rash or infection/Itching/Desquamation	81 (48.8)	38 (61.2)	21 (46.7)	9 (42.8)	13 (34.2)	0.058
Back pain	54 (32.5)	25 (40.3)	14 (31.1)	8 (38.1)	7 (18.4)	0.139
Alopecia (diffuse)	53 (31.9)	23 (37.1)	8 (17.8)	10 (47.6)	12 (31.6)	0.063
Respiratory tract infection + Otitis	45 (27.1)	17 (27.4)	18 (40.0)	3 (14.3)	7 (18.4)	0.072
Anorexia	43 (25.9)	21 (33.8)	11 (24.4)	5 (23.8)	6 (15.8)	0.243
Genital/Urinary tract infection/STI	38 (22.8)	22 (35.5)	5 (11.1)	3 (14.3)	8 (21.0)	0.018
Insomnia	30 (18.0)	10 (16.1)	7 (15.6)	4 (19.0)	9 (23.7)	0.760
Gastritis/Ulcer/Gastroesophageal reflux disease	27 (16.2)	11 (17.7)	7 (15.5)	4 (19.0)	5 (13.2)	0.918
Malaria	23 (13.8)	10 (16.1)	3 (6.7)	2 (9.5)	8 (21.0)	0.241
Moderate acute malnutrition	19 (11.4)	10 (16.1)	6 (13.3)	1 (4.7)	2 (5.2)	0.277
Cardiopathy/Valvulopathy/Tachycardia	19 (11.4)	7 (11.3)	6 (13.3)	2 (9.5)	4 (10.5)	0.966
Amenorrhea[a]	7 (10.1)	0 (0.0)	3 (16.7)	0 (0.0)	4 (26.7)	0.045
Arterial hypertension	12 (7.2)	4 (6.4)	4 (8.8)	1 (4.7)	3 (7.8)	0.928
Diarrhea/Gastroenteritis	9 (5.4)	5 (8.0)	2 (4.4)	0 (0.0)	2 (5.3)	0.545
Tinitus/Hearing loss	5 (3.0)	1 (1.6)	3 (6.7)	0 (0.0)	1 (2.6)	0.370
Severe acute malnutrition	2 (1.2)	1 (1.6)	1 (2.2)	0 (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)	0.754
Any ocular complication	94 (56.6)	41 (66.1)	22 (48.8)	11 (52.3)	20 (52.6)	0.353
Uveitis	58 (34.9)	26 (41.9)	10 (22.2)	8 (38.0)	14 (36.8)	0.213

[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.

Table 4: Univariate and multivariable analyses: Risk factors for sequelae of acute Ebola virus disease among survivors enrolled in the MSF follow-up program, Freetown, Sierra Leone.

	Uveitis		Any ocular complication		Arthralgia	
	OR N=166 (95% CI)	OR Adjusted[a] N=65 (95% CI)	OR N=166 (95% CI)	OR Adjusted[a] N=65 (95% CI)	OR N=166 (95% CI)	OR Adjusted[a] N=65 (95% CI)
Age						
0-15	0.40 (0.16- 0.98)*	0.16 (0.02-1.17)	0.81 (0.37-1.75)	0.90 (0.23-3.47)	0.18 (0.07-0.45)*	0.08 (0.016-0.41)*
16-30	1	1	1	1	1	1
31+	0.91 (0.43-1.93)	2.39 (0.40-14.16)	0.99 (0.47-2.08)	2.22 (0.44-11.14)	0.91 (0.33-2.52)	0.61 (0.08-4.47)
Sex						
Male	1	1	1	1	1	1
Female	1.55 (0.81-2.96)	4.38 (0.87-22.0)	1.36 (0.73-2.53)	1.93 (0.58-6.46)	1.42 (0.67-3.02)	0.35 (0.71-1.80)
ETC of discharge						
MSF Prince of Wales	1	-	1	-	1	-
Other	0.96 (0.51-1.83)	-	1.11 (0.60-2.06)	-	0.76 (0.36-1.58)	-
Time to first follow-up						
0-30 days	1	1	1	1	1	1
31-60 days	0.39 (0.16-0.93)*	0.18 (0.04-0.84)*	0.48 (0.22-1.07)	0.49 (0.16-1.45)	0.90 (0.36-2.22)	1.45 (0.34-6.15)
61 – 90 days	0.85 (0.30-2.35)	-	0.56 (0.20-1.53	-	1.75 (0.44-6.81)	-
≥90 days	0.80 (0.35-1.85)	-	0.56 (0.24-1.29)	-	0.93 (0.36-2.44)	-
Joint pain during follow-up						
No	1	1	1	1	1	1
Yes	1.15 (0.53-2.51)	1.90 (0.34-10.63)	0.99 (0.47-2.07)	1.07 (0.28-4.05)	1.15 (0.53-2.51)	2.33 (0.38-14.1)
Cycle threshold value[b]	0.95 (0.84-1.07)	0.99 (0.82-1.21)	1.02 (0.91-1.15)	1.05 (0.92-1.21)	0.99 (0.87-1.13)	1.04 (0.88-1.24)
Days hospitalized[b]						
1-10 days	1	1	1	1	1	1
11+ days	1.10 (0.45-2.83)	0.37 (0.08-1.64)	0.83 (0.34-2.02)	0.72 (0.22-2.32)	0.97 (0.35-2.67)	1.88 (0.45-7.75)
Red/injected eye in ETC[b]						
No	1	1	1	1	1	1
Yes	3.34 (1.18-9.45)*	10.4 (1.91-57.5)*	2.22 (0.77-6.38)	2.84 (0.81-9.86)	2.18 (0.63-7.58)	1.53 (0.30-7.61)

Abbreviations: OR, odds ratio; CI, confidence interval; ETC, ebola treatment center.

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

[b]Only survivors from MSF Prince of Wales; Cycle threshold value, N=77; Days hospitalized, N=81; Red/injected eye in ETC, N=70.

*Confidence intervals that do not overlap the null values of OR=1, p-value ≤0.05.