Post-Ebola Sequelae Among Child Ebola Survivors in Sierra Leone

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Abstract

Introduction

: There is limited data regarding the long-term health effects of child survivors of the 2013–2016 West African Ebola virus disease (EVD) outbreak. Here, we assess post-Ebola complications among EVD child survivors by comparing the self-reported symptoms between EVD child survivors and their close household contacts over one year after the end of the outbreak.

Methods

Child EVD survivors(n = 159) and their close contacts(n = 303) were enrolled in Western and Eastern Sierra Leone. Demographic and self-reported symptoms data were collected using an interviewer-administered questionnaire. We compared a list of self-reported symptoms between EVD child survivors and their close household contacts using backward stepwise logistic regression.

Results

Child EVD survivors were more likely to be orphans compared to their controls. Musculoskeletal, ocular, auditory and neurological symptoms were more prevalent among Ebola survivors than their close contacts ($p < .001$). Joint pain and headache were the most common self-reported symptoms, and child survivors and their contacts. Joint pain (AOR = 2.633; 95% CI1.313-5.278, $p = 0.006$), eye pain (AOR = 4.559,95%CI: 2.156–9.639, $p < 0.001$) hearing loss (AOR = 3.849, 95%CI: 1.151–12.871, $p = 0.029$), memory impairment (AOR = 7.763,.95%CI: 1.339–45.007 $p = 0.022$), mood changes (AOR = 5.070, 95%CI: 2.350-10.939, $p < 0.001$) were more common among survivors than their contacts.

Conclusion

Our data suggest that child EVD survivors have higher odds than their close contacts to suffer from post-Ebola musculoskeletal, ophthalmic, auditory and neurological impairment more than a year after the end of the EVD outbreak. Routine screening, treatment and monitoring of these symptoms is required to prevent long-term disability among child Ebola survivors.

Background

The recent West African Ebola virus disease (EVD) epidemic began in 2013 in Guinea and spread rapidly to Liberia and Sierra Leone. These three were classified as countries with intense transmission by the WHO due to their high infection rates[1]. The total number of cases and deaths from this epidemic is the highest ever recorded for Ebola, with 28,652 and 11,325 respectively, of which 28,616 cases and 11,310 deaths were reported from these countries[2]. The first confirmed case of EVD in Sierra Leone was

documented in May 2014 in the Eastern District of Kailahun and subsequently spread to all thirteen Districts. The total number of confirmed, probable, and suspected EVD cases in Sierra Leone recorded at the end of the West African outbreak was 14,124[2]. Of these, the total number of cases confirmed was 8,706 cases, and the total number of deaths was 3,956[2].

Due to the magnitude of the epidemic, West Africa has been left with many Ebola survivors, approximately 10,000 reported by WHO. However, it has become apparent that Ebola survivors carry the risk of severe complications, including but not limited to chronic joint and muscle pain, fatigue, anorexia, hearing loss, blurred vision, headache, sleep disturbances, psychiatric and mood disorders, short-term memory problems, arthralgia, and uveitis, among others [3–5]. From the WHO's Interim Guidance for clinical care for survivors of EVD, all the systems in the body are affected by the sequelae of Ebola[6]. The major challenge facing survivors is often the need for specialized services, which are not readily available in the affected countries [7, 8]. These include ophthalmic care and mental health services.

While documentation of complications in adults has improved, it is becoming apparent that there is limited information on complications available for child survivors. Among nations affected by the outbreak, Sierra Leone recorded the highest rate of children infected with Ebola, with 20% of confirmed infections aged 14 years or younger [9]. Case fatality rate (CFR) in children younger than five years has been highest in the West African EVD epidemic, with children less than one year having a case fatality ratio of 90% and under-five having a CFR of 80%[10].

To date, there is limited existing literature on the sequelae of Ebola in children, although the physical, psychological, and social impacts of the disease on this vulnerable group is significant [4]. There are no known age-specific interventions to prevent complications in child survivors. The dearth of information on complications in EVD child survivors creates a gap in the literature on Ebola and limits the ability to offer appropriate follow-up and care to these children. Therefore, it is of utmost importance to identify, evaluate child survivors of Ebola in Sierra Leone, create a cohort that can be followed up, and inform preparation for future outbreaks. This study assesses post-Ebola complications among EVD child survivors by comparing the self-reported symptoms between EVD child survivors and their close household contacts.

METHODOLOGY

Methodology

General Settings

Sierra Leone has an estimated population of 7 million, of whom approximately 70% live below the poverty line[11]. The country's indices for maternal and infant mortality are among the worst globally, ranking respectively fifth and eleventh. This is partly due to the period of civil conflict (1991–2002) that devastated the country and its health system. Even before the Ebola outbreak, there were only two doctors and 17 nurses per 100000 population, most of whom were situated in urban areas[11]. The

health infrastructure is tiered into tertiary hospitals, district hospitals, and peripheral health units (PHUs) designed to deliver primary health care. The PHUs include community health centres (CHCs), community health posts (CHPs) and maternal and child health posts (MCHPs)[12].

The study was conducted in the Western Area urban and rural districts in the Western region and Kenema district in the Eastern region of Sierra Leone. The Western Area is the wealthiest region in Sierra Leone, having the largest economy, financial and cultural centre, as well as the seat of the country's national government. It is divided into two districts: Western Area Rural and Western Area Urban. Kenema district is the district headquarter of the Eastern Province of Sierra Leone. These two regions were regarded as epicentres, with up to 4000 cases of Ebola reported [2].

Study design, population, sampling, and data collection

This was a cross-sectional study among EVD child-adolescent survivors and their close contacts, between January and April 2017. EVD child survivors aged 5-17years were enrolled in this study. We excluded those less than five years and those who could not properly respond to some of the questions. EVD child survivors were identified based on a list obtained from a registry of Ebola survivors from the Ministry of Social Welfare, Gender and Children's Affairs (MSWGCA) and Sierra Leone Association of Ebola Survivors. Potential controls were child contacts of EVD child-adolescent survivors from the same household who were not infected with Ebola. They were within the same age group as EVD child survivors. These controls provided a healthy cohort with similar genetic, socioeconomic, and environmental characteristics to the EVD child survivor cohort. A maximum of two household contact was chosen for every child EVD survivor.

Data variables and source

Trained personnel were used to collect information from survivors, contacts or parents/guardians of survivors and controls using a pre-designed questionnaire. The questionnaire was designed based on the available literature regarding post-Ebola sequelae among adult Ebola survivors[3, 13-15]. Data was collected through interviewer administered format and interviews were conducted in Creole (widely spoken language in Sierra Leone).at participants' place of residence. The following information were collected; age, sex (male vs female), weight, geographical location (Western Area Urban, Western Area Rural and Kenema, social status (orphan vs non-orphan), education level (no formal education, primary and secondary), how many times they were hospitalised during and after the Ebola outbreak, history of any disease before EVD. We also collected data on post-Ebola symptoms of EVD based on the available literature [3, 4, 14-16].

Statistical analysis

Data from filled questionnaires were coded and analysed using Statistical Package for Social Sciences (SPSS) for Windows, Version 23 (Chicago Inc.). Categorical and continuous variables were represented in frequency, percentages, mean, and standard deviation, respectively. Bivariate analysis using Chi-square

or Fisher exact tests were used to establish an association between survivors and controls. A backward stepwise multivariate regression analysis was used to determine the odds of presenting with a particular post-Ebola symptom between child survivors and their contacts. Age, sex, gender, weight, education level, geographical location, and social status (orphan vs non-orphan) were considered potential cofounders and controlled when conducting the regression analysis.

Ethical approval

Permission to conduct this study was obtained from the Sierra Leone Scientific and Ethics Review Committee, Ministry of Health and Sanitation, Freetown. Verbal and written informed parental/guardian consent were obtained for all participants using the WHO Research Ethics Committee (WHO ERC) template for research involving children.

Results

One –hundred and fifty-nine Ebola survivors cases and 303 closed contacts were recruited. Ebola survivors were likely to be greater than 16 years than other age groups. There was no statistically significant difference between survivors and controls with respect to gender. Survivors were more likely to be orphans compared to their controls. Likewise, Child Ebola survivors were more likely to have attained secondary education than their controls. Please see Table 1 below for details

Table 2 shows the clinical profile of Ebola survivors and their close contacts. Musculoskeletal, ocular, auditory and neurological symptoms were more prevalent among Ebola survivors compared to their close contacts. Headache [n= 139(86.9)] followed by Joint pain[n=101(63.1%)] were the most common self-reported symptoms among child survivors. Similarly, headache [n=220 (72.8%) followed by joint pain [n=58(19.2%)] were the most prevalent among contacts.

Table 3 provides a summary of the self-reported symptoms between survivors and their close contacts. Joint pain (AOR=2.633; 95% CI1.313-5.278, p=0.006), hearing loss (AOR=3.849, 95%CI: 1.151-12.871, p=0.029), memory impairment (AOR=7.763,.95%CI: 1.339-45.007 p=0.022), mood changes (AOR=5.070, 95%CI: 2.350-10.939, p<0.001) were more common among survivors than their contacts. In addition, child survivors were three or more times (AOR=6.774, 95% CI: 3.513-13.062, p<0.001) more likely to be hospitalised after the end of Ebola than their contacts.

Discussion

The study presents findings of the first-ever analysis of post-Ebola symptoms among paediatric Ebola survivors. Our analysis indicates that paediatric Ebola survivors have higher odds of being hospitalised after the end of Ebola outbreak and presenting with specific clinical symptoms than their contacts.

Musculoskeletal, ocular, auditory and neurological symptoms were more prevalent among Ebola survivors compared to their close contacts. Joint pain and headache were the most common self-

reported symptoms among child survivors. Our findings align with previous studies conducted among adult survivors in West Africa [13-17]. We observed that paediatric Ebola survivors were more likely to present with joint pain, eye pain, and hearing loss compared to their contacts. Long term musculoskeletal, ophthalmic, and auditory sequelae have been demonstrated among adult Ebola survivors [17-19]. As in adult survivors, musculoskeletal, ophthalmic auditory sequelae can limit their ability to live a normal life. Routine screening, treatment and monitoring of these symptoms is required to prevent long-term disability among child Ebola survivors. The interim guidance for clinical care of EVD survivors published by WHO could serve as a guide to managing these symptoms[6]

Our data has shown that paediatric Ebola survivors were more likely to be at higher odds of presenting with memory loss and loss of sensation than their contacts. Such subjective post-EVD neurological impairment is a common complication observed in previous studies among adult Ebola survivors [14, 17, 20, 21]. Mood changes were also observed among this cohort of Ebola survivors. This could be an indication of common mental disorders, such as severe depression, post-traumatic stress disorder and anxiety. Such symptoms of psychological distress have been reported among adult Ebola survivors [4, 22, 23]. Such sequelae may be an indication of a long-term neurological abnormality and mental health disorder. Children presenting with such cognitive impairment and potential mental health disorders must have access to psychiatric assessment and, if possible, treatment to prevent long term neurological damage and mental health disorders.

Our multivariate analysis indicates that child survivors were more likely to be hospitalised than their contacts after the end of the Ebola outbreak. This may be due to the weak health status of child survivors, which may be attributed to the high physical and psychological trauma they experienced during admission and after discharge from the Ebola treatment centres [3, 4].

Study Limitations

A key limitation of our study is the reliance on self-reports of the clinical manifestations among survivors and their contacts. Also, serological screening among contact was not done to rule out asymptomatic EVD infection, although asymptomatic EVD infection is uncommon in West Africa [24]. Notwithstanding these limitations, our study presents the first-ever statistically significant case-controlled findings on post-Ebola symptoms among paediatric Ebola survivors. Further studies are needed to confirm our findings and to have a better insight into the underlying pathogenesis that explains the clinical manifestations observed in this study.

Conclusion

Our study has shown that like adults Ebola survivors, paediatric Ebola survivors have higher odds of developing musculoskeletal, ophthalmic, auditory and neurological impairment following discharge from an Ebola treatment centre. Psychological issues in the form of mood changes were evident among this cohort of Ebola survivors. Further research is required to address our study limitations, to confirm our

findings, and at the same time improve our understanding of the clinical pathology underlying the occurrence of the clinical complications among paediatric Ebola survivors.

List Of Abbreviations

AOR- Adjusted Odd Ratio

EVD Ebola Virus Disease

PHU- Peripheral Health Units

CHP- Community health Post

MCHP-Maternal Child health Post

Declarations

Ethics approval and consent to participate

Permission to conduct this study was obtained from the Sierra Leone Scientific and Ethics Review Committee, Ministry of Health and Sanitation, Freetown. Verbal and written informed parental/guardian consent were obtained for all participants.

Consent for publication

Not Applicable

Availability of data and materials

All data are available within manuscript and it will be made available upon reasonable request from the corresponding author.

Competing interests

The authors declared no competing interest whatsoever.

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Author contribution:

Study conceptualisation: CA and SRS

Protocol design: CA, PBJ, AJB and SRS

Data Collection: CA, AVSB and AJB

Statistical analysis: PBJ

Manuscript writing: CA, PBJ, AJB

Draft of final manuscript: CA, PBJ, AJB, AVSB and SRS

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Tables

Table 1
socio-demographic profile of survivors and contacts

Characteristics	Variables	Ebola Survivor n (%) N = 159	Control n (%) N = 303	Total n (%)	p-value
Age	Mean	11.08 ± 3.68	9.56 ± 3.38		< 0.001
Sex	Male	78(48.8)	148(49.0)	226(48.9)	0.958
	Female	82(51.2)	154(51.0)	236(51.1)	
Weight*	Mean	38.5	32.6		< 0.001
Location of Participant	Western Area Urban	76(47.5)	142(47.0)	218(47.2)	0.983
	Western Area Rural	53(33.1)	99(32.8)	152(32.9)	
	Kenema	31(19.4)	61(20.2)	92(19.9)	
Social Status	Orphan	83(51.9)	43(14.2)	126(27.3)	< 0.001
	Non-Orphan	77(48.1)	259(85.8)	336(72.7)	
Education Level	None	16(10.0)	46(15.2)	62(13.4)	< 0.001
	Primary	94(58.8)	223(73.8)	317(68.6)	
	Secondary	50(31.3)	33(10.9)	83(18.0)	
History of illness prior to Ebola	Yes	47(29.4)	49(16.2)	96(20.8)	0.001
	No	113(70.6)	253(83.8)	366(79.2)	
How many times visited hospital before Ebola	Less than three times	140(88.6)	280(93.0)	420(91.5)	0.107
	Three or more times	18(11.4)	21(7.0)	39(8.5)	
How many times hospitalised during Ebola Outbreak	Less than three times	141(88.1)	295(97.7)	436(94.4)	< 0.001
	Three or more times	19(11.9)	7(2.3)	26(5.6)	
How many times hospitalised after the end of Ebola	Less than three times	51(32.5)	249(83.3)	300(65.8)	< 0.001
	Three or more times	106(67.5)	50(16.7)	156(34.2)	

*Student t-test was used to determine the difference between means

Table 2
clinical profile of Ebola survivors and contacts

Clinical Symptoms	Variables	Ebola Survivor n (%) N = 159	Contacts n (%) N = 303	Total n (%)	p-value
Chest Pain	Yes	47(29.4)	28(9.3)	75(16.2)	< 0.001
	No	113(70.6)	274(90.7)	387(83.8)	
Joint Pain	Yes	101(63.1)	58(19.2)	159(34.4)	< 0.001
	No	59(36.9)	244(80.8)	303(65.6)	
Muscle Pain	Yes	57(35.6)	39(12.9)	96(20.8)	< 0.001
	No	103(64.4)	263(87.1)	366(79.2)	
Eye Pain	Yes	68(42.5)	19(6.3)	87(18.8)	< 0.001
	No	92(57.5)	283(93.7)	375(81.2)	
Eye Redness	Yes	55(34.4)	19(6.3)	74(16.0)	< 0.001
	No	105(65.6)	283(93.7)	388(84.0)	
Dry eyes	Yes	29(18.1)	11(3.6)	40(8.7)	< 0.001
	No	131(81.9)	291(96.4)	422(91.3)	
Blurred Vision	Yes	22(13.8)	3(1.0)	25(5.4)	< 0.001
	No	138(86.3)	299(99.0)	437(94.6)	
Sensitive to light	Yes	40(25.0)	12(4.0)	52(11.3)	< 0.001
	No	120(75.0)	290(96.0)	410(88.7)	
Ringing in the ear (Tinnitus)	Yes	32(20.0)	11(3.6)	43(9.3)	< 0.001
	No	128(80.0)	291(96.4)	419(90.7)	
Hearing Loss	Yes	33(20.6)	9(3.0)	42(9.1)	< 0.001
	No	127(79.4)	293(97.0)	420(90.9)	
Epigastric Reflux	Yes	13(8.1)	2(0.7)	15(3.2)	< 0.001
	No	147(91.9)	300(99.3)	447(96.8)	
Blood or mucus in the stool	Yes	15(9.4)	9(3.0)	24(5.2)	0.003
	No	145(90.6)	293(97.0)	438(94.8)	
Headache	Yes	139(86.9)	220(72.8)	359(77.7)	0.001
	No	21(13.1)	82(27.2)	103(22.3)	

Clinical Symptoms	Variables	Ebola Survivor n (%) N = 159	Contacts n (%) N = 303	Total n (%)	p-value
Memory Impairment	Yes	29(18.1)	3(1.0)	32(6.9)	< 0.001
	No	131(81.9)	299(99.0)	430(93.1)	
Loss of sensation	Yes	23(14.4)	6(2.0)	29(6.3)	< 0.001
	No	137(85.6)	296(98.0)	433(93.7)	
Tremor	Yes	17(10.6)	4(1.3)	21(4.5)	< 0.001
	No	143(89.4)	298(98.7)	441(95.5)	
Seizures	Yes	5(3.1)	5(1.7)	10(2.2)	0.302
	No	155(96.9)	297(98.3)	452(97.8)	
Mood Changes	Yes	72(45.0)	18(6.0)	90(19.5)	< 0.001
	No	88(55.0)	284(94.0)	372(80.5)	

Table 3
Multivariate regression analysis of post–Ebola clinical symptoms

Self-reported symptoms	Variables	AOR	95%CI	p-value
Joint pain	Yes	2.633	1.313–5.278	0.006
	No	1		
Muscle pain	Yes	0.452	0.193–1.059	0.068
	No	1		
Eye pain	Yes	4.559	2.156–9.639	< 0.001
	No	1		
Hearing loss	Yes	3.849	1.151–12.871	0.029
	No	1		
Memory impairment	Yes	7.763	1.339–45.007	0.022
	No	1		
Loss of sensation	Yes	7.321	1.256–42.680	0.027
	No	1		
Seizures	Yes	0.120	0.013–1.112	0.062
	No	1		
Mood changes	Yes	5.070	2.350-10.939	< 0.001
	No	1		
Hospitalised after the end of Ebola outbreak	Yes	6.774	3.513–13.062	< 0.001
	No	1		
Hospitalised during the Ebola outbreak	Yes	3.257	0.862–12.303	0.082
	No	1		

AOR- Adjusted odds ratio