Inpatient signs and symptoms and factors associated with death in children aged 5 years and younger admitted to two Ebola management centres in Sierra Leone, 2014: a retrospective cohort study

Tejshri Shah, Jane Greig, Linda Margaretha van der Plas, Jay Achar, Grazia Caleo, James Sylvester Squire, Alhaji Sayui Turay, Grace Joshy, Catherine D'Este, Emily Banks, Florian Vogt, Kamalini Lokuge

Summary

Background **Médecins Sans Frontières (MSF) opened Ebola management centres (EMCs) in Sierra Leone in Kailahun in June, 2014, and Bo in September, 2014. Case fatality in the west African Ebola virus disease epidemic has been highest in children younger than 5 years. Clinical data on outcomes can provide important evidence to guide future management. However, such data on children are scarce and disaggregated clinical data across all ages in this epidemic have focussed on symptoms reported on arrival at treatment facilities, rather than symptoms and signs observed during admission. We aimed to describe the clinical characteristics of children aged 5 years and younger admitted to the MSF EMCs in Bo and Kailahun, and any associations between these characteristics and mortality.**

Methods **In a retrospective cohort study, we included data from children aged 5 years and younger with laboratory-confirmed Ebola virus disease admitted to EMCs between June and December, 2014. We described epidemiological, demographic, and clinical characteristics and viral load (measured using Ebola virus cycle thresholds [Ct]), and assessed their association with death using Cox regression modelling.**

Findings **We included 91 children in analysis; 52 died (57·1%). Case fatality was higher in children aged less than 2 years (76·5% [26/34]) than those aged 2–5 years (45·6% [26/57]; adjusted HR 3·5 [95% CI 1·5–8·5]) and in those with high (Ct<25) versus low (Ct≥25) viral load (81·8% [18/22] *vs* 45·9% [28/61], respectively; adjusted HR 9·2 [95% CI 3·8–22·5]). Symptoms observed during admission included: weakness 74·7% (68); fever 70·8% (63/89); distress 63·7% (58); loss of appetite 60·4% (55); diarrhoea 59·3% (54); and cough 52·7% (48). At admission, 25% (19/76) of children were afebrile. Signs significantly associated with death were fever, vomiting, and diarrhoea. Hiccups, bleeding, and confusion were observed only in children who died.**

Interpretation **This description of the clinical features of Ebola virus disease over the duration of illness in children aged 5 years and younger shows symptoms associated with death and a high prevalence of distress, with implications for clinical management. Collection and analysis of age-specific data on Ebola is very important to ensure that the specific vulnerabilities of children are addressed.**

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Manson Unit, Médecins Sans Frontières, London, UK (T Shah MSc, J Greig PhD, J Achar MBBS, G Caleo MD, K Lokuge PhD)**; Department of Paediatrics, St Mary's Hospital, Imperial College NHS Healthcare Trust, London, UK** (T Shah)**; Department of Medical Oncology, Antoni van Leeuwenhoek Hospital, Netherlands Cancer Institute, Amsterdam, Netherlands** (L M van der Plas MD)**; Ministry of Health and Sanitation of Sierra Leone, Kailahun, Sierra Leone** (J S Squire MD)**; Ministry of Health and Sanitation of Sierra Leone, Bo, Sierra Leone** (A S Turay MD)**; National Centre for Epidemiology and Population Health, Research School of Population Health, Australian National University, Canberra, Australia** (G Joshy PhD, C D'Este PhD, E Banks PhD, K Lokuge)**; and Médecins Sans Frontières, Brussels, Belgium** (F Vogt MSc)

Correspondence to
Tejshri Shah, Manson Unit, Médecins Sans Frontières, 10 Furnival Street, London EC4A 1AB, UK
tejshrishah@gmail.com

Introduction

By Aug 16, 2015, 27 952 cases of Ebola virus disease had been reported in Guinea, Liberia, and Sierra Leone as part of the west Africa Ebola epidemic.[1] Of the 15 186 people with laboratory-confirmed infection, 20% were aged 14 years or younger.[1] Sierra Leone had the highest rate and absolute number of confirmed infections in this age group.[1]

Evidence from all age groups shows that case fatality is highest in children under 5 years, suggesting that young children have different risks than do older children, adolescents, and adults.[2] However, data on the epidemiological, clinical, and laboratory features of Ebola virus disease in children are scarce.[3–5] Furthermore, clinical data across all age groups published from the 2013–16 outbreak have captured historic symptoms reported on arrival to Ebola management facilities, and omitted ongoing signs objectively observed by clinical staff during admission.[2,6–8] Data on signs collected during admission have the potential to inform clinical practice and to improve our understanding of Ebola virus disease.

The first ever case of Ebola virus disease in Sierra Leone was reported in May, 2014, in Kailahun, a rural district in the southeast of the country, adjacent to the Guéckédou region of Guinea where the outbreak originated. Médecins Sans Frontières (MSF) opened a purpose-built Ebola management centre (EMC) in Sierra Leone in Kailahun in June, 2014. The EMC initially

Panel: Research in context

Evidence before this study

We searched PubMed for articles relating to Ebola in children from Jan 1, 1976, to Aug 15, 2015. Search terms used were "paediatric" OR "pediatric" OR "child" AND "Ebola". There is a paucity of clinical information on children with Ebola virus disease and we found no articles that described clinical features in young children during their inpatient stay. There are two relevant papers for Ebola virus disease in children. The first is a report by Mupere et al[3] on 168 inpatients under 18 years of age affected by Sudan Ebola virus in 2000–01 in Uganda. It includes only 20 patients with laboratory confirmed Ebola virus disease and does not disaggregate information by age. The second paper by the WHO Ebola Response Team presents the West African epidemic age-specific outcomes and symptoms reported on arrival, but not during hospital admission. An important finding in this paper was that children younger than 5 years have the highest case fatality.

Added value of this study

Our study focuses on the clinical features of Ebola virus disease in children aged 5 years and under. We describe, for 91 children, symptoms and outcomes confirmed by health-care workers during hospital admission in Ebola management centres. This study describes symptoms in relation to outcome and early symptoms. Signs significantly associated with death were fever, vomiting, diarrhoea, and distress. Hiccups, bleeding, and confusion were observed only in children who died. Our paper highlights the frequency (63·7%) of distress during admission. The case fatality in this cohort was 57·1% (52/91). Case fatality was highest in children under 2 years (76·5% [26/34]) and in those with an Ebola virus cycle threshold <25 (81·8% [18/22]) indicating a higher viral load, compared with those patients with a cycle threshold ≥25 (45·9% [28/61]) at admission.

Implications of all available evidence

This study confirms the high rates of death in children younger than 2 years with Ebola virus disease, especially those with a high viral load at presentation. It gives insight into the symptom profile in younger children with Ebola virus disease and encourages the broader recognition of distress as a relevant symptom in this group, with implications for symptom relief in children and, possibly, for the improvement of training of clinical staff in distress and pain recognition and management. We highlight the dearth of knowledge on how Ebola virus disease affects younger children. Programme managers and researchers should aim to collect and analyse age-specific data so that the specific vulnerabilities of young children are not overlooked.

received patients from across the entire country and patients often endured long and debilitating journeys to reach the centre. In September, 2014, a second MSF EMC was opened in Bo, which is the second largest city in Sierra Leone and centrally located with good road access.

In this study, we report on children with Ebola virus disease admitted to the two EMCs in Kailahun and Bo. Given the paucity of clinical information on Ebola virus disease in young children and their vulnerability, we aimed to describe the clinical characteristics of children aged 5 years and under, report their signs and symptoms on arrival and during admission, and assess the factors associated with death.

For the **study protocol** see http://fieldresearch.msf.org/msf/handle/10144/583990

Methods

Patients

We included all children aged 5 years and younger admitted to the Kailahun and Bo EMCs between June and December, 2014, with confirmed Ebola virus disease. We used WHO case definitions to screen people before testing.[9] A suspected case was a person who had a sudden onset of fever and contact with a person with suspected, probable, or confirmed Ebola or a dead or sick animal. Or any person with sudden onset of high fever and at least three of the following symptoms: headache, lethargy, anorexia (loss of appetite), aching muscles or joints, stomach pain, difficulty swallowing, vomiting, difficulty breathing, diarrhoea, hiccups; or any person with inexplicable bleeding.

We used data that were collected for clinical purposes and anonymised before analysis. This study met the criteria of the MSF Ethics Review Board for exemption from ethics review for retrospective analyses of routinely collected programmatic data.[10] The study protocol is available on the MSF open repository.

Procedures

Workers completed a case investigation form as soon as was feasible after the arrival of each patient and recorded demographic characteristics, exposure history, date of symptom onset, and past and present symptoms. Age was corroborated with family members whenever possible. After assessment of clinical status and epidemiological information, patients were admitted to "suspect/probable" tents and underwent a blood test, and people who tested positive for Ebola virus were transferred to a "confirmed" tent. Tests were done by laboratories run by the Public Health Agency of Canada (Kailahun) and the US Centers for Disease Control and Prevention (Bo).

Cases were confirmed by presence of Ebola virus RNA, detected with quantitative RT-PCR with two amplification targets in venous or capillary swab blood. The latter involved a capillary sample that was collected onto a cotton swab because venous sampling was not always feasible in young children. Results were accessible for 83 patients as cycle thresholds (Ct), a measure inversely related to viral load. The translation of Ct into viral load was not identical between the two laboratories. We tested whole blood samples before discharge for patients who were clinically convalescing (that is, no vomiting or