



Ebola virus disease: a commentary on clinical presentation and outcomes in children

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In the last half a century, Ebola virus disease (EVD) has had remarkable epidemiological transitions. In the East African Country of Uganda, it first appeared as a less aggressive viral illness in the early 1970s and was an infrequent disease of little public health significance. However, in the last three decades, it reemerged as a severe viral illness with progressive and increasing frequency of outbreaks, especially in the Central and Western African regions (1-3). Moreover, the public health significance of EVD climaxed in the 2014 outbreak in West Africa, which led the WHO to declare a global emergency (4). EVD has no pathognomonic features since its clinical presentation is generally non-specific (2). In most resource limited settings, the primary recognition of the illness is a report of sudden community outbreak of a *rare* or *unusual fatal illness* (2). Formally the respective ministries of health with their partners especially the CDC and/or WHO usually constitute epidemic investigation team. Laboratory confirmation of at least one clinical case triggers the declaration of an epidemic outbreak in that country or region. It is important to remember that EVD is a very fast progressing, aggressive and highly contagious disease. It requires immediate medical attention in specialized isolation care units. Collection of real time prospective clinical data is difficult and often unsafe for the researcher. Most clinical data on EVD therefore are retrospective studies.

The clinical case definitions that follow a first confirmed case are often pragmatic including; suspected, probable, contact or confirmed cases (2,5). The intent is to have a case definition with the highest possible sensitivity to maximize

case-catch rates in the community. The earlier and accurate the recognition of an outbreak is made the better. However, corresponding robust public health responses in order to achieve earlier control and limit further spread of the epidemic must follow index case reports.

Shah *et al.*, recently published an article on 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 (5). Like many other authors before, they noted a paucity of data on paediatric EVD. Their study highlighted key features on inpatient clinical features and prognosis. Nonetheless, as opposed to previous paediatric EVD series where data were at admission, their data were from a cohort of PCR confirmed cases at and through admission.

These authors for the first time attempted a comprehensive description of the inpatient clinical features and their respective outcomes. They reported a highest case fatality in children, especially those less than 2 years of age (5). The social context of high dependency of young children (<5 years) on adults may be the main predisposing factor to prolonged intense contact with the Ebola virus (2). In addition, Shah *et al.* (5) reported data on only PCR confirmed cases, yet most earlier paediatric series on EVD included low specific clinical criteria for case definitions (2). The admission features they reported including fever, weakness, distress, vomiting and diarrhea—are common clinical features in patients with shock, a known predictor of poor outcomes in children with acute febrile critical illness (6,7). Furthermore, these authors

reported rare features in childhood EVD including bleeding, hiccups and confusion all suggestive of multisystem failure, especially that these were terminal clinical features (5).

Earlier series reported 100% of confirmed cases had fever; with temperature of $>38^{\circ}\text{C}$ (8,9). For the first time, Shah *et al.* found 70.8% (63/89) had fever ($\geq 38^{\circ}\text{C}$) (5). This points at two possibilities: Firstly, that the data from earlier series (8,9) may have been as a result of different strain of EVD to that reported in Sierra Leone in 2014 (5), but needs to be confirmed. Secondly, the clinical stage at which the patients presented to the various treatment centres may have varied. It is plausible that patients presenting to the treatment centre early in the illness on the basis of contact alone as a risk factor may not have clinical features but test positive because of they are in the incubation period. Conversely, in very advanced stages, patients with shock may actually have hypothermia as a physiological defense mechanism (10). Exploring history of fever in 48–72 hours prior to admission would have given insight into the consistency or otherwise of fever in EVD that would accurately put in perspective the 25% (19/76) of the afebrile patients in the sierra Leone cohort. Another remarkable difference in this series is that there were no differences in mortality disaggregated by gender (5). On the contrary, earlier series, especially those in Uganda indicated that more females were affected compared to their male counterparts (9). These contrasts suggest differences in girl child household chores, and household patient care roles in the two geographical regions, backgrounds and ethnicities.

Shah *et al.* (5), nonetheless, have brought new insight into the descriptions of the paediatric clinical spectrum of EVD during the course of illness in admitted children aged 5 years and younger. In addition, they have shown clinical features associated with high mortality. Importantly, they have demonstrated collection and analyses of data disaggregated by age as very significant in advancing knowledge on specific vulnerabilities of children of different age strata.

At this stage, evidence from all published series on EVD seems to piece together clinical presentation at admission (8,9), and during admission (5). However, there is a gap in knowledge on early/preadmission clinical features and how they influence outcomes. Moreover, there is still missing information including; how incubation period of EVD in children differs from that in adults? Outcomes with treatment involving fluids especially in light of use of fluid boluses in febrile shocked children (6,7), need evaluation. Additionally, the

role of different EVD strains or mixed infections needs further research. In all EVD series, however, all children with Ebola RT-PCR confirmed cases had history of contact (8,9); and none as index case.

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