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Ebola Outbreak: Knowledge to Act

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Abstract

The persistence, spread and escalation of Ebola virus disease (EVD) ravaging West Africa is now a serious global threat. The epidemic has resulted in unprecedented number of deaths and cases including health care workers in countries with the poorest staffing patterns. This article provide a general background information on EVD and specifically address what is known and what need to be done at individual and society level to mitigate its effect. The epidemic appears to be attributed and sustained by negative socio-economic factors, notably extreme poverty, poor health infrastructure and disintegrated health care system. The extreme social-economic factors have created an atmosphere of fear, panic, helplessness, hopelessness further perpetuating the epidemic. There is need for the international community to scale up support for the affected countries to mitigate stress, restore supplies, economic activities and instill hope. Global concerted efforts, resource mobilization and support will contain and slow down the outbreak preventing international disaster and globalization of the outbreak.

Keywords: Ebola virus disease; EVD; Social economic; Globalization; Support

Introduction

The persistence, spread and escalation of Ebola virus disease (EVD) outbreak in Guinea, Liberia, Sierra Leone, Nigeria and recently Democratic Republic of Congo (DRC), Senegal [1] and now USA, Mali and Spain is worrisome. The epidemic appears to cause the greatest devastation in nations with extreme poverty and negative socio-economic factors. Save for Nigeria and Senegal, which have been declared ebola free, the rest of the affected nations are mainly struggling. This state of affairs have caused substantial level of panic in the global community, but also triggered response activities and resource mobilization in preventing further spread.

Epidemiology of the current Ebola outbreak

The outbreak is the largest ever, it began in December 2013 and first confirmed in March 2014 in Guinea [2]. Indeed, public health experts are in consensus that the problem is much bigger possibly because of gross under reporting [3].Historically, the worst hit countries have had vicious forms of conflict, war and instability with resultant depletion of health care system, health infrastructure, professionals, in addition to illiteracy and poor health statistics [4-6]. The situation has been compounded by fear, panic and feeling of discrimination, high illiteracy driving the belief that Ebola is a result of witchcraft [4]. The outbreak has resulted in unprecedented number (13628) of cases and deaths (4986), among them health workers in the line of combat (Table 1). This is a painful loss, given that this important human resource is already scarce in the Ebola ravaged countries [7,8].

Country	All Cases	Confirmed cases	Proportion of confirmed cases (%)	Deaths	Case fatality rate (%)
Guinea	1667	1409	84.5	1018	61.1
Liberia	6535	2515	38.5	2413	36.9
Sierra Leone	5338	3778	70.8	1510	28.3
Totals	13540	7702	56.9	4941	36.5
Countries with imported cases					
Nigeria	20	19	95	8	40
Mali	1	1	100	1	100
Spain	1	1	100	0	0
USA	4	4	100	1	25
Totals	26	25	96.2	10	38.5
Unrelated ebola outbreak					
DRC	62	-	-	35	56.5
Global totals	13628	7727		4986	
Source: WHO Ebola response roadmap situation report 2014					

Table 1: Distribution of Ebola cases and case fatality rates by country

Ebola virus the cause of EVD was first reported in 1976 following simultaneous outbreaks in Yambuku, Zaire (now the Democratic Republic of Congo (DRC), and Nzara town in Sudan [9]. Since then, more than 20 outbreaks have been documented [10], the current being

the largest on the basis of deaths, cases, duration, geographical spread, resource mobilization [3], fear, response and media coverage. The virus (named after river Ebola in DRC), is an RNA type which belongs to the family of filoviruses [11,12]. There are five distinct ebolavirus sub-types namely; Zaire, Bundibugyo, Taï Forest, Sudan and Reston. The later is pathogenic to non-human primates only [13]. The strain causing the current epidemic carries 97% homology to Zaire ebolavirus samples found in the DRC and Gabon [2]. This strain has previously been attributed with the highest mortality (90%), but the current outbreak has an estimated case fatality rate of 70.8% [1]. The case fatality rate differs from one country to the other depending of classification of cases and elimination of some by experts for failure to meet case definitions after review (Table 1).

The Ebola virus is a zoonotic pathogen, with outbreaks originating from an animal reservoir and possibly involving other intermediary species [14]. Fruit bat appears to be the culpable reservoir, although that linkage has not been confirmed [15]. In most instances, the outbreak has emerged from geographically restricted rural areas. In early 2014 for example, the outbreak emerged in a remote region of Guinea near the borders with Sierra Leone and Liberia [14]. This was similar to the infections seen in DRC, though the outbreak was unrelated to the West African type (no contact or travel history to West Africa). Interesting, a positive history of the case having slaughtered a bush animal was given, corroborating the fact that Ebola virus is a zoonotic pathogen. The circulation of Ebola virus among humans is rare, possibly explaining the intermittent and unpredictable nature of the outbreaks [14]. Human infections however, can be acquired from intermediate mammalian hosts, including domestic pigs and primates. Transmission to humans occurs through direct contact with tissue or bodily fluids from an infected animal. Onward human to human transmission is through direct contact with blood, secretions (sweat, sputum, vomit, diarrhea, blood, urine, vaginal fluids or semen), organs, or other body fluids of infected persons (alive or dead) [3]. Furthermore, touch of beddings or other inanimate objects contaminated with bodily fluids result in transmission. Person to person transmission may also occur through direct inoculation by contaminated instruments such as needles, pins, razors blades [16,17] and the so called nasocomial transmission through contaminated needles and syringes [18]. Patients become infectious once they are symptomatic (2 to 21 days after infection), and may persist even after symptoms subside (virus persists in body fluids). The current epidemic appears to be exclusively sustained by person-to-person transmission through physical contact [14].

Pathogenesis of Ebola viral disease

The pathogenesis of EVD is not well-understood, however, the immune system and vascular bed appears to be a direct target [19,20-25]. Studies in nonhuman primates have shown that Ebola virus replicates in monocytes, macrophages, and dendritic cells [24]. The virus has also been isolated in endothelial cells, fibroblasts, hepatocytes, and adrenal cells, following in situ hybridization and electron microscopy. The virus disseminates to lymph nodes, the liver, and the spleen. Patients with severe disease produce extremely high levels of inflammatory cytokines, which destroy normal tissue and microcirculation, leading to profound capillary leakage, renal failure, and disseminated intravascular coagulation [25]. Inhibition of the type I interferon response seems to be an important pathogenic pathway of Ebola. Dysregulation of the coagulation cascade and production of pro-inflammatory cytokines by macrophages leads to shock and multi-organ failure and dysfunction in the terminal phase [15]. There may be some inflammatory response and significant lymphocyte apoptosis, which leads to lymphopenia and seems to be a marker of prognosis.

Clinical features of EVD

The EVD is a syndrome that can rapidly lead to death within days following the onset of symptoms. The incubation period is minimum 2 days and 21 days maximum, with average 8 days for the majority [26]. The case fatality rate has been documented between 50-90% [11,26]. Initially the clinical symptoms are nonspecific, with sudden onset of fever, chills, myalgia, and malaise. This makes the diagnosis difficult because the symptoms may be confused with those of endemic diseases in Africa, such as malaria, typhoid fever, bacterial meningitis, or Lassa fever [14]. The initial phase is followed by flu-like symptoms (rhinorrhoea, cough, and shortness of breath); gastrointestinal symptoms (diarrhea, nausea, vomiting and abdominal pain); a maculopapular rash has also been described [26] and, finally hemorrhagic symptoms in the most severe cases (Table 2). Hemorrhagic complications occur in fewer than half of infected persons, and gross bleeding is relatively rare. Poor prognosis is associated with the development of shock, encephalopathy, and extensive hemorrhage [15,26]. Hematological and blood chemistry profile of importance include leukopenia, thrombocytopenia, elevated levels of aminotransferase and prothrombin, and partial thromboplastin times with presence of fibrin split products indicating diffuse intravascular coagulation [15].

Cases	Definition	Signs and Symptoms
Probable case	Any suspected person evaluated by a clinician (or died) from suspected Ebola and had epidemiological link to a confirmed case.	Sudden onset of high grade fever, Myalgia and malaise Headache, Abdominal pain Diarrhea Muscles pain General body weakness Bleeding (Internal/ external
Suspected case	Any person (alive or dead) who had sudden onset of high grade fever , had contact with a suspected, probable or confirmed Ebola case or sick animal or any person with high grade fever with at least three of the following symptoms; headache, vomiting, anorexia, loss of appetite diarrhea, lethargy, stomach pain, joint pain, difficult in swallowing, breathing difficulties, hiccups or any person with unexplained bleeding tendencies	
Confirmed case	Any probable or suspected case whose sample test positive for Ebola virus by laboratory techniques.	
Source: WHO Ebola response roadmap situation report 2014		

Diagnosis of EVD

Diagnostically, early EVD symptoms mimic other endemic diseases common in tropics because of similarities in clinical presentation [8]. It is therefore critically important, to obtain careful and prompt travel history for the last 3 weeks given the incubation period of 21 days. In the affected countries, it is important to ask about travel to the outbreak area, history of contact with cases and participation in burial of Ebola corpses. The criteria for suspecting EVD include typical symptoms such as high grade fever of sudden onset, profound

weakness, and diarrhea. Blood specimens usually begin to test positive on polymerase-chain-reaction–based (PCR) diagnostics 1 day before symptoms appear [14]. When the diagnosis is suspected, PCR and antigen detection by enzyme-linked immunosorbent assay (ELISA) are the most useful tests. The ELISA test elicits specific IgG and IgM antibodies (presence of IgM antibody indicates recent infection). More so, both ELISA and PCR tests are important for antigen detection in blood, serum or organ homogenates. Postmortem diagnosis is typically through immunohistochemical examination of formalin-fixed skin biopsy specimens [18,27]. Serial testing for the cases and samples should be submitted with clinical notes for ease of interpretation of the test results. The test results should be made available within 24 hour to guide public health decisions and actions [27]. Unfortunately, these tests are only available in referral centers or national reference laboratories and have not been readily available in remote areas of Africa where most outbreaks have occurred.

Treatment and EVD case management

There is no approved specific treatment or vaccine for EVD. However, enhanced case management in isolated units should be initiated once EVD is suspected. Symptomatic and supportive management is the mainstay for treatment of patients with EVD [28,29]. These interventions if instituted aggressively together with intensive care support, significantly improve survival, reduce case fatality and minimize nosocomial transmission [3,14]. Evidence from the two American cases that were evacuated with EVD from Liberia to receive first notch care in Atlanta, USA with impressive results of 100% recovery and zero transmission support the aforesaid. Such care should involve advanced hemodynamic monitoring and interventions including; volume repletion, blood pressure maintenance and other life supporting activities notably oxygenation, pain control, nutritional support, treatment of secondary bacterial infections and preexisting conditions thus reducing case fatality significantly [14].

Prevention and control measures

In massive outbreaks, as is the case with West Africa, establishment of emergency operations/response centers, as well as communication and social mobilization programs are required. These programs help the affected populations understand and comply with infection control measures, while they also assist health authorities understand how the measures can be introduced in a culturally sensitive way [3]. Confirmed as well suspected case management offers an opportunity for systematic surveillance, training and supervision of health workers on clinical evaluation and appropriate interventions, infection control and barrier nursing practices to minimize health facility transmissions. Health workers and those at risk of infection (burial, morticians, drivers and care takers) should be provided with protective materials (masks, gloves, plastic aprons, gum boots and head wear). They should be trained on downing, handling and removal of the personal protective equipment (PPE) during and after the procedure to minimize transmission. Health workers should be trained in counseling and guidelines for the proper discharge of patients, as discharge and management of convalescent patients is critical in the management of the epidemic. To prevent/reduce EVD transmission in the community, safe burial practices including identification and instituting trained burial teams and providing guidelines for burial should be observed. Additionally, Ebola corpses should be safely transported from the isolation units in body bags to the burial ground. To avoid further spread of infection through transporting the dead bodies over long distance, suspicious community deaths should be buried in the community by the trained burial team [27].

Quick systematic response to EVD should involve, public sensitization, early diagnosis, patient isolation, contact tracing, strict adherence to bio-safety guidelines in laboratories, barrier nursing procedures and use of PPE by all health care workers, disinfection of contaminated objects and areas, and safe burials 3 are the cornerstone for Ebola infection containment. These measures serve to interrupt transmissions in both health facility and community settings. To achieve them, substantial funding is required. In the current epidemic albeit slow initial response, a well-coordinated international response has been initiated and sustained so far. The declaration by WHO on the current outbreak as a public health emergency of international concern (PHEIC) [3] triggered sustained efforts toward mitigating and containing the epidemic. Some bold measures such as mobilization of resources to a tune of millions of US dollars towards buying of personal protective equipment (PPE), awareness and laboratory diagnosis among others have been implemented. Furthermore, the national governments of the affected countries have declared EVD a national disaster, raising the response level and increasing resource mobilization, and establishing a disaster response mechanism and banning of international travel by the affected persons and contacts [3]. The national governments instituted stringent measures of screening all people arriving and departing from air and sea ports and closure of borders to support control measures.

Social-economic effects of EVD outbreak

Ebola outbreak has interrupted human activities through forced closure/slowdown of social and economic activities such as schools, market places and cross-border trade, mining and agricultural sectors in the affected areas. Furthermore, major airlines from Western, Asia and Africa countries have suspended their flights in response to the WHO call for containment of the epidemic, pressure from citizens and travel advisories [8,3]. These factors put together though critical in the outbreak containment appear ineffective. The interventions have perpetuated the isolation of already stressed communities through economic marginalization and a possible cause of economic meltdown. Financial, human resource support and mobilization for the affected countries is a critical measure in combating the outbreak. This approach will guarantee economic survival, logistical (including hospital) supplies, awareness creation thus mitigating fear, panic and feeling of discrimination hence promoting case tracking and surveillance.

Finally, the epidemic has brought to the fore key issues; first, the need to invest and develop health care infrastructure and human resource capability for responding to epidemics. Second, there is need to invest in biomedical research for drugs and vaccines for diseases endemic in low economic countries as a social responsibility by the multinational drug companies as a matter of priority. This may be hampered by limited knowledge on EVD including sequencing, evolutionary pattern and trend of the virus. Third, the ethical debate in health care got exciting; this is in light of patients with EVD who were put on experimental drug (ZMapp) that had shown effectiveness in non-human primates [19] whether or not the therapy contributed to their recovery is difficult to conclude. This together with military support for ebola outbreak raises ethical issues and/or knowledge of such non-conventional method applications for humanitarian purposes. This epidemic however, has also seen a decision made to accelerate the trials for vaccine against Ebola on health subjects in

USA, Britain and two African Nations. This portends that this may be the last epidemic to be managed without a vaccine.

Despites all the international and local efforts against the outbreak, indications are that the epidemic is accelerating, and spreading, with DRC and Senegal, Spain, Mali and USA being the latest culprits. This is a call for all the players to accelerate the efforts for EVD surveillance. The first case in Senegal is of interest because the affected was a college student who escaped surveillance. As colleges in the North America and Europe prepare to welcome a global cohort of international students, it is important to increase surveillance and be more vigilant to detect cases as early as possible to avoid globalization of the virus. It is important for the cases in the current epidemic to be analyzed to establish demographical patterns to understand the impact of the outbreak on different population groups especially women and children already bearing heavy burden in the poor countries.

Conclusion

The current EVD outbreak calls for improvement of health care infrastructure for all African nations. In addition, there is need to address intra- and inter-country poverty and inequalities in holistic approach. Laboratory infrastructure and capacities require to be upgraded for timely confirmation of cases and appropriate response. Training, retraining and support of the health care providers on basics of infection control is required. Enhanced resource mobilization and investment in research on drugs, vaccines and rapid test kits to address re-emerging and emerging diseases such as EVD is required as a priority global response. Disease surveillance at the community level with functional reporting system to healthcare, with supported response mechanism will help reduce the outbreak and case fatality rates in future. Social- economic support to family and communities that have been affected, as well as economic recovery of affected countries need to be addressed.

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