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Review article

Ebola hemorrhagic fever outbreaks: strategies for effective epidemic management, containment and control

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ABSTRACT

Ebola hemorrhagic fever, caused by the highly virulent RNA virus of the *filoviridae* family, has become one of the world's most feared pathogens. The virus induces acute fever and death, often associated with hemorrhagic symptoms in up to 90% of infected patients. The known sub-types of the virus are *Zaire*, *Sudan*, *Taï Forest*, *Bundibugyo* and *Reston* Ebola viruses. In the past, outbreaks were limited to the East and Central African tropical belt with the exception of Ebola Reston outbreaks that occurred in animal facilities in the Philippines, USA and Italy. The on-going outbreak in West Africa that is causing numerous deaths and severe socio-economic challenges has resulted in widespread anxiety globally. This panic may be attributed to the intense media interest, the rapid spread of the virus to other countries like United States and Spain, and moreover, to the absence of an approved treatment or vaccine.

Informed by this widespread fear and anxiety, we analyzed the commonly used strategies to manage and control Ebola outbreaks and proposed new approaches that could improve epidemic management and control during future outbreaks. We based our recommendations on epidemic management practices employed during recent outbreaks in East, Central and West Africa, and synthesis of peer-reviewed publications as well as published "field" information from individuals and organizations recently involved in the management of Ebola epidemics.

The current epidemic management approaches are largely "reactive", with containment efforts aimed at halting spread of existing outbreaks. We recommend that for better outcomes, in addition to "reactive" interventions, "pre-emptive" strategies also need to be instituted. We conclude that emphasizing both "reactive" and "pre-emptive" strategies is more likely to lead to better epidemic preparedness and response at individual, community, institutional, and government levels, resulting in timely containment of future Ebola outbreaks.

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Introduction

Ebola hemorrhagic fever (EHF) or Ebola virus disease (EVD) is the human disease caused by infection of the single stranded RNA viruses of the genus '*Ebola*' and family '*Filoviridae*'. Ebola virus was discovered in 1976, following coinciding outbreaks in Zaire, now Democratic Republic of the Congo (DRC), and Sudan.[1,2] EVD usually begins with an acute fever, causing death following hemorrhagic symptoms in up to 90% of cases depending on the viral species.[1,2] The known species include *Bundibugyo Ebolavirus* (*BEBOV*), *Sudan Ebolavirus* (SEBOV), Zaïre *Ebolavirus* (*ZEBOV*), Reston *Ebolavirus* (*REBOV*) and *Côte D'Ivoire Ebolavirus* (*CIEBOV*), also known as, *Taï Forest Ebolavirus* (*TAFV*). The *REBOV* strain has caused no human deaths so far, but has been lethal to chimpanzees, gorillas and monkeys.[3,4]

In terms of pathogenicity, SEBOV strain leads to case fatality rates of 40–60%, *ZEBOV* rates range from 60% to 90%, while the *BEBOV* strain is associated with fatality rates of 25%. The *CIEBOV* subtype has been implicated in a single non-fatal human case.[2,4] Generally, this high fatality rate, the international spread of the virus across borders, including the possible use of the viral isolates as a possible tool for bioterrorism make EVD an important public health concern of global proportions. Consequently, Ebola outbreaks lead to widespread fear, anguish and hysteria, locally and internationally, due to media attention, commerce, travel and tourism.[3,5]

Typically, EVD leads to rapid suppression of the immune system, triggering systemic inflammatory response causing impaired vascular, coagulation and immune systems functioning, resulting in multiple organ failure, hypovolemic shock and death.[2,5] Since its discovery in 1976, no effective vaccine or post-exposure treatment exists to date. Hence, the current disease management plan consists of supportive therapy to revive infected patients, minimizing infection transmission, and calming anxious populations.[2,3] These interventions often require interdisciplinary efforts instituted at both community and healthcare institutions.

In this paper, we discuss the epidemiology, clinical features and mode of transmission of Ebola virus. We also highlight epidemic response efforts instituted in recent outbreaks in East, Central and West Africa. We recommend strategies for improved epidemic management during and in-between outbreaks. The paper is based on synthesis of original research and review papers indexed in MEDLINE, Scopus, PubMed, CINAHL, Science Direct, and Google Scholar databases, published between January 2000 and September 2014, as well as data collected during a doctoral research study conducted in Uganda between June and July 2013.

To reflect current practices and highlight specific aspects of epidemic management, we have also included substantial amounts of recent "field" information from individuals and organizations involved in the recent outbreaks, in the form of online resources, newspaper articles, press releases and clinical guidelines. The resources and publications used were obtained from data bases using combinations of the Medical Subject Headings (MeSH) and related search terms, "Ebola hemorrhagic fever"; "Ebola virus disease"; "filoviridae infections"; "Ebola epidemics"; "communicable disease control"; "case management"; "disease surveillance"; "epidemiology" and "disease management". Peer-reviewed articles published in the last decade in English that focused on Ebola and Marburg was prioritized.

Focus of the study

This article briefly introduces the reader to Ebola virus disease, the various strains and the common signs and symptoms of the disease, including current epidemic management strategies. The paper ends with recommendations for improved epidemic management strategies based on the lessons learnt from outbreaks in East, Central Africa and West Africa.

Mode of transmission

The exact transmission mode of Ebola viruses from their natural reservoir to humans or non-human primates remains largely unknown,[2,6] although most outbreaks appear to be zoonotic. In laboratory animals, the virus can initiate infection following ingestion, inhalation or passage through breaks in the skin.[4,7] In non-human primates, experiments have also shown that transmission can occur through droplet inoculation of the viruses into the mouth or eyes.[8]

In humans, outbreaks usually occur following person-to-person transmission involving direct contact with the mucous membranes or broken skin with contaminated blood, vomitus, urine, feces, and semen from infected persons.[7,9] During outbreaks, it has been shown that direct contact among humans occurs during funerals, as part of ritual handling of corpses, as a major mode of interfamilial transmission.[8,10] In addition, healthcare workers are at risk of infection if they care for Ebola patients without appropriate protective measures due to shortages and poor infrastructure or following exposure to patients with unrecognized Ebola virus disease.[5,11]

Contrary to the belief that the Ebola virus is confined to the rain forest of Central Africa, the on-going outbreak in West Africa[3,11] has shown that the virus can spread rapidly and widely, covering large areas, in this case Guinea, Liberia, Sierra Leone, Nigeria, Senegal, Mali, and USA. The factors implicated in this spread are fear, denial, misinformation, mistrust, concealment, and rumor. These resulted in contacts and infected persons to avoid or escape from surveillance systems or treatment centers,[3,11] or relatives hiding symptomatic family members or taking them to traditional healers. Such unregulated movement of infected persons across borders amplifies Ebola epidemics, exacerbated by inadequate surveillance systems and medical isolation centers,[11,12] and persistent high-risk cultural practices like consumption of bush meat and funeral rituals where physical contact occurs with the deceased patient.[2,13]

In addition to human to human contact, direct contact with infected wild animals such as gorillas or chimpanzees during hunting, butchering and while preparing meat has been a significant source of infection to humans especially in the DRC, Gabon, and Uganda.[2,13] Apart from contact with infected non-human primates, human exposure to bat secretions or excretions has also been demonstrated to be a potential route

for acquisition of Marburg and Ebola viruses following studies done in the DRC and Uganda.[14] During epidemics, nosocomial infection associated with medical procedures such as intravenous site insertions and surgeries have amplified filovirus epidemics, especially where rules of universal precautions, barrier nursing, and infection control are not well observed.[5,9] These examples further demonstrate that transmission of Ebola viruses can occur through contaminated patient care equipment and supplies. Ebola virus has also been transmitted following accidental infection of workers in Biosafety-Level-4 (BSL-4) facilities during investigational studies.[15] These transmission modes and observations in Uganda, the DRC, and West Africa confirm that large Ebola epidemics occur after patients enter weak healthcare systems, where barrier nursing and epidemic management practices are inadequate due to the lack of facilities.[5,12,13]

Clinical manifestations

Infected patients present with severe headache, shivers, sore throat, muscle aches, weakness and hiccups in the early stages of the illness, following an incubation period of 2–21 days.[6,16] As the disease progresses, patients develop nausea, vomiting, difficult breathing, abdominal pain, diarrhea, pharyngitis, conjunctivitis, organ dysfunction, hypovolemic shock, and bleeding from body orifices and intravenous injection sites, eventually ending up in death.[2,8] For survivors, the process of recovery is very slow, characterized by complaints of severe loss of weight, scaly skin, loss of appetite, sexual weakness and inflammation of the testes in male survivors. In addition, visual and hearing difficulties, tiredness, mental stress, muscle and bone pains, including menstrual disturbances in female survivors, are also common.[2,8,9]

Strategies for effective epidemic management and containment

The management of Ebola outbreaks continues to be complicated by several challenges and shortcomings. These difficulties relate to clinical management of patients, contact tracing, disease surveillance, logistics, laboratory testing, communication, resistance, panic and hysteria in affected populations. This is further complicated by the fact that the natural reservoir of the virus remains unknown,[2,6] thereby negatively impacting primary prevention.

In absence of primary prevention, epidemic management focuses mainly on educating the masses and instituting secondary strategies during outbreaks and in the aftermath. The success of secondary prevention strategies requires good understanding of the public's views about Ebola as a disease. Understanding people's views and perspectives helps health workers, government officials and development partners to design effective approaches to educate the masses about Ebola and its effects, including how to deal with its social consequences.[9,17,18]

The learnt lessons from previous outbreaks indicate that incorporating community's perspectives and beliefs helps in gaining their support and to demystify the epidemic, resulting in reduced fear, panic and antisocial sentiments during an Ebola outbreak[3,16,19] In fact, incorporating the perspectives of local populations into national epidemic response efforts, with support from international and local experts and local and international partners, leads to better epidemic control, particularly in resource challenged environments.[11,17,19]

Currently, the most dominant outbreak management strategy may be classified as "*post outbreak interventions*". However, the continuing outbreaks in East, Central and West Africa demonstrates the urgent need for health workers, international agencies, development partners and governments to institute not only the usual "*post outbreak interventions*", but to also emphasize additional response strategies, which we refer here as "*constant interventions*". This strategy permits dealing with the reality and threat of Ebola decisively and effectively.

"*Post outbreak interventions*" are "reactive" actions undertaken at community or institutional levels to mitigate the spread of on-going epidemics, while "*constant interventions*" are "pre-emptive" steps taken at individual, community and institutional levels to boost preparedness and readiness to deal with future epidemics. "*Constant interventions*" can help to significantly boost health workers' understanding of the human aspects of the illness, by illuminating hidden aspects of what the illness means to the locals and how their notions about Ebola blend with cultural beliefs and practices and how these impact epidemic responses in the future.[20]

Post outbreak interventions

Post outbreak interventions are "preventive and corrective measures" instituted by epidemic response teams once an outbreak has begun. It aims to prevent further spread of infection, and encourage individuals and communities to engage in activities that can slow and halt the spread of the virus.[21] The interventions vary widely from basic hygienic practices such as hand washing and cleaning of clothing and hunting tools to proper cooking of meals especially of meat products, all to minimize contamination. The strategy also emphasizes timely case management as well as mobilization of communities in at-risk areas against consumption of bush meat, including wild hoofed animals, primates, rodents and bats.[6,11,21]

Post outbreak interventions further encourages timely identification of probable patients, transferring suspects to designated medical facilities, monitoring suspects and enforcing infection control measures in health facilities and communities. When properly implemented, this strategy considerably slows down epidemics, eventually leading to its mitigation.[2,10,17] In recent outbreaks in East, Central and West Africa, the post outbreak interventions used may be classified under *active disease surveillance*, *laboratory confirmation*, *case management*, *social mobilization*, *education and training*, *resource mobilization* as well as *communication*.

The practice of '*active disease surveillance*' encourages healthcare practitioners working in urban and rural communities and hospitals to document, report, and promptly refer contacts to isolation centers, ensuring swift detection and control of new infections. This case-by-case reporting of '*suspects*' to national or regional Ebola response teams allows their

prompt follow-up and referral to isolation centers, as well as to assess the scope of the epidemic.[2,20]

The intervention of '*laboratory confirmation*' is mandatory when an epidemic is suspected, up to the point where the epidemic is confirmed and then diagnosis can be based on clinical manifestations.[8–10] Setting up a field-screening laboratory to handle samples safely, securely and timely is mandatory to facilitate prompt diagnosis and to guide mode of patient care.[10,18]

The mode of '*case management*' depends on whether the patient belongs to the surveillance categories of "alert", "suspect", "probable" or "confirmed"; which ranges from suspected contact with an infected person to laboratory confirmation of Ebola infection. When a person is declared "*confirmed*" case, they are immediately isolated, followed by speedy initiation of supportive therapy.[9,19] When the patient makes full recovery, proper discharge is mandatory to ensure that there is unhindered reintegration back into their home communities, which normally occurs due to fear and stigma following the hospitalization of Ebola patients and contacts.[10,11] Case management also involves establishing safe burial practices,[19,20] including identifying suitable burial grounds, training burial teams and developing guidelines to ensure safe burial.[22] Further, case management entails ensuring that no direct contact occurs with the deceased and burials are restricted to trained teams in full personal protective equipment.[10,19]

The steps of "*social mobilization*" are employed to facilitate multisectoral collaboration, epidemic preparedness and response because of the ability to influence both health workers and community members to actively participate in epidemic control.[18,23,24] The media has been used for social mobilization, especially local radio stations to educate communities for rapid and meaningful response in affected areas.[9,10] Social mobilization has also incorporated the use of community drama groups at public places such as markets, schools and worship places to attract mass attention and then to pass key messages to win peoples' confidence, including fighting social stigma.[20] Documentary films and educative posters have been used to discourage "high-risk" practices, such as handshakes, large gatherings, healing practices and traditional burial rituals to curtail rates of infection and promote epidemic response.[10,22,24]

Educating and training healthcare practitioners and community resource persons during outbreaks has been another major intervention employed to prepare communities to participate in surveillance and epidemic management activities.[19,22] This intervention is vital because correct management of epidemic control activities leads to appropriate community response.[10,22,25] Besides providing information about epidemic response, "*personal safety training*", is also emphasized with special focus on safe wearing and removal of full-body equipment. The training also emphasizes the "*buddy system*" of working in pairs, where colleagues watch over each other, when wearing protective gears and when providing patient care to ensure no steps are missed and their safety is guaranteed.[21,22,26] The education and training sessions ensure that there is both knowledge and readiness to respond to ongoing epidemics.

Resource mobilization after an outbreak is vital because the fight against Ebola epidemics is highly resource intensive. This may be in form of medical and support staff, finances, vehicles, food, clothing, personal items or as hospital and laboratory equipment and supplies.[8,9,27] To succeed in resource mobilization, there is need for multisectoral collaboration between ordinary citizens, civil society organizations, political and faith based organizations, as well as local and international development partners and government departments.[10,27,28]

Another vital aspect of epidemic control that significantly affects the outcome of outbreak management is the communication strategy. Field experiences from previous outbreaks indicate that epidemic related information should be communicated to the public in ways that build, maintain or restore trust and respect local cultures and country norms.[29,30] Information sharing between stakeholders, such as government departments, development partners, religious bodies, training institutions, local leaders and the public leads to timely interventions. Improved communication is thus critical because it facilitates resource identification and mobilization, social mobilization, education and training, surveillance and case management as well as helping to re-integrate survivors and contacts into families.[19,27,28]

A key element of improved communication is early integration and involvement of the media to help with shaping the public's perception about the epidemic and to educate them on disease prevention and control mechanisms.[18,27,28] Improved communication also necessities obliging media agencies, both local and international media outlets, to communicate, to the public in a timely manner, vital epidemic information in ways that instil confidence and not fear, encouraging and mobilizing key stakeholders in the community, country and globally to respond to any health threats, including actively contributing to outbreak management.[18,30,31]

Early involvement of the media was noted to result in more accurate and timely reporting,[16,18,19] creating awareness for infection prevention. This in turn prompts community action including rushing suspected cases to isolation centers.[10,19] This increased awareness also encourages individuals to avoid contact with 'suspect' cases and inspires better compliance with and support for epidemic control guidelines leading to mitigation of the epidemic.[19,27,31]

Constant interventions

In addition to the reactive, '*post outbreak interventions*', that characterizes current epidemic management, we propose that the continued sporadic occurrence of Ebola epidemics in East, Central and West Africa requires a more holistic way to deal with the threat of the epidemic. We suggest a strategy consisting of "*pre-emptive*" steps, termed, '*constant interventions*' approach, that should be undertaken at individual, community and institutional levels following an epidemic and to be continued in the aftermath, that is in-between the outbreaks.

Emphasizing such "pre-emptive" strategy is likely to improve the epidemic readiness, particularly that of "at-risk" populations and government agencies in 'high-risk' countries. When properly implemented, such holistic measures help to enhance the knowledge related to Ebola outbreaks, as well as preparedness and readiness of populations, healthcare

institutions and key government departments to respond in a timely manner should an epidemic emerge.

In essence, '*constant interventions*' are intended to keep populations and institutions in 'high-risk' areas ready, fully prepared and constantly aware of the risk of Ebola outbreak recurrence. Such preparedness is likely to result in rapid epidemic response should an outbreak occur, considerably enhancing the possibility of timely epidemic control. We recommend that the "*constant interventions*" strategy employed should be informed by the public's perceptions and beliefs about Ebola and should address any gaps that exist in their understanding of the illness. This implies that interventions carried out in-between outbreaks should be relevant and evidence based,[18,19] further maintaining that during "*constant interventions*", health teams should address misinformation, rumors, beliefs, and peoples' peculiar experiences with previous Ebola outbreaks. This is vital not only for "*neutralizing*" negative perceptions about Ebola and its management, but rather to help in confidence building and motivating communities to trust more in the health care workers and the outbreak related services.[19,27,31]

Preferably, these interventions should be implemented at both individual and family (human or micro) and institutional and governmental (macro) levels. This "binary" approach has the capacity to enhance individuals', families', institutions' and countries' epidemic preparedness and response in the event of new outbreaks. The "*constant interventions*" at individual/family (micro) level should focus largely on information provision, sharing best practices and health education to increase knowledge levels.[19,31] In contrast, at governmental/institutional (macro) level, the "*constant interventions*" should seek to improve the capacity and readiness of various departments that usually provide essential services required to respond to outbreaks.

We recommend that to enhance institutional effectiveness, health practitioners in 'at-risk' areas and countries need to be kept constantly up-to-date with current epidemic response strategies, reinforced through regular seminars and workshops.[18] The "*constant interventions*" strategy ensures that health institutions infrastructure are "*epidemic ready*". This readiness entails making significant improvements in health facility infrastructure such as improving isolation units, diagnostic laboratories and instituting infection control facilities and procedures.[10] Such interventions are particularly vital in Ebola prone areas of East, Central and West Africa where sporadic outbreaks have occurred.[11,19] When properly implemented, these "*constant interventions*" can ensure that health workers, community leaders and the public are properly informed about the true nature of Ebola including recommendations for outbreak containment aimed at early case detection, reporting and clinical management. These interventions also ensure that vital health and related service institutions in at-risk communities and countries are fully prepared and ready to respond to an imminent epidemic.

Conclusions

Ebola virus disease is a serious public health concern because of its frightening nature and the large number of deaths associated with it, resulting from multi-organ and multi-system failure and hypovolemic shock.[2,6,9] Currently, no globally approved treatment or vaccine exists. This lack has contributed to the failure to control the on-going Ebola outbreaks affecting large parts of West Africa, despite efforts of a global coalition coordinated by the World Health Organization.[3,11] The scale of the outbreak has pressured world players and the pharmaceutical players to speed up the human trials of available candidate vaccines,[3,32,33] and necessitated the use of previously untested drugs on Ebola patients,[34] leading to unprecedented ethical challenges.[35,36] In the absence of a recognized definitive vaccine and treatment, the best option to deal with Ebola outbreaks is designing more responsive approaches to manage on-going epidemics and to promote epidemic preparedness and readiness among individuals, non-governmental organizations and government departments in high-risk countries.[2,18,19]

In Ebola prone areas and particularly during outbreaks, it is vitally important that health workers, international agencies, development partners and governments establish epidemic management strategies early and such efforts should continue well into the aftermath of outbreaks. Incorporating both "*post outbreak interventions*" and "*constant interventions*" offers a real chance for health teams and governments to deal with the threat of an on-going and future Ebola outbreaks in a timely and decisively way. The advantage of this "binary" approach is that while "*post outbreak interventions*" enhance communities and health care institutions' capacity to mitigate further spread of an on-going epidemic, the '*constant interventions*' at individual, community and institutional levels deepen their understanding about Ebola, thereby enhancing overall epidemic preparedness and response.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical approval

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