

Ebola Virus Disease (EVD): An Unprecedented Major Outbreak in West Africa

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Abstract

Ebola virus disease (EVD), one of the deadliest virus diseases has affected a number of African countries periodically ever since 1976. The present epidemic of EVD is being regarded as an unprecedented major outbreak of west Africa involving Liberia, Sierra Leone, Guinea and Nigeria. About 9,000 people have contracted the disease and nearly 4,500 had fatal outcome. Both morbidity and mortality is likely to increase in coming months due to paucity and non-availability of specific anti-viral drugs and vaccines. Mass education, preventive measures and international commitment on war footing can help contain the present epidemic. However, the epidemic is likely to have significant long lasting economical, social and political after effects.

Keywords: Ebola virus disease; Major outbreak; West Africa

Editorial

Ebola virus was first reported from southern Sudan and northeastern Zaire, the present day Democratic Republic of Congo (DRC) as an outbreak of hemorrhagic fever [1]. The virus derives its name from Ebola river (which is a headstream of Mongala river, a tributary of Congo river) where the first outbreak of the disease was reported. Over the last 38 years periodically many epidemics of Ebola virus disease (EVD) have been reported from various African countries [2-9]. Whereas during 1990s and in the early years of the present century the worst hit countries have been DRC, Sudan, Uganda, Gabon and Congo-Brazzaville, the present epidemic of west Africa has been unprecedented in terms of mortality and morbidity. Fortunately but surprisingly reasons being ambiguous, the 13 years period between 1980 to 1993 had been silent with no EVD cases reported. The present outbreak could be traced back to December 2013 when a 2 year old child (the first index case) belonging to the village of Meliandou, Gueckedou prefecture, Guinea died of the disease on 6th December, 2013. Thereafter, over the months the disease spilled over to major urban and capital towns of Guinea, Sierra Leone, Liberia and Nigeria infecting about 9,000 people and taking a toll of nearly 4,500 at the time of this write up but there are speculations that both cases and deaths are underestimated. On 8th August 2014, WHO declared the present epidemic to be a public health emergency of international concern. Occasional cases of EVD have more recently been reported in USA and western Europe. The number of EVD patients may even go beyond 20,000 in coming months. Even though Nigeria is the most populous African country, only 20 cases and 8 EVD deaths have so far been reported as compared to the other three countries struggling with the disease. Senegal reported only a single case who recovered from the disease but no further cases occurred thereafter. Both Nigeria and Senegal may be declared Ebola-free by the WHO if no further cases occur there after 42 days (double the incubation period) of the last reports. But there is no place for complacency and the EVD may return from the affected areas if there is any laxity in the surveillance and the preventive measures. Although the fatality in the present outbreak is about 55 -60%, ebola virus is one

of the most dreadful viruses and may have fatality up to 90 %. It belongs to the family *Filoviridae*. Historically, the earliest virus of this family capable of causing human disease was Marburg virus (MARV) which resulted in 31 cases of hemorrhagic fever with 7 deaths of laboratory workers in 1967 who were processing kidneys from African green monkeys procured by Germany from Uganda.

Ebola virus is a filamentous (filament or thread like) single stranded, enveloped, negative sense RNA virus 80 nm in diameter and about 800-1000 nm in length. Some particles may even be exceptionally much longer. They may be circular, U or 6- shaped. The envelope is composed of lipid bilayer with peplomers surrounding a helical tubular nucleocapsid. The RNA is about 19 kb in size. The virus can be cultured in Vero and other standard cell lines. It multiplies in the cytoplasm of the cells producing large inclusion bodies. The virions are released from the plasma membrane by budding. The genus Ebola virus has five different species named after the places from where the initial cases were reported. Accordingly they are Zaire ebola virus (ZEBOV), Sudan ebola virus (SEBOV), Cote d' Ivoire ebola virus (CIEBOV), Bundibugyo ebola virus (BEBOV) and Reston ebola virus (REBOV). REBOV was discovered when several monkeys imported from Philippines into USA became ill and died at a holding facility at Reston, Virginia, but REBOV has never been found to be pathogenic for humans. MARV, another filamentous virus, though similar to ebola virus in morphology and clinicopathological features is antigenically different from it but has also caused outbreaks of hemorrhagic fever with fatality over 80% in DRC in 1998-2000 and Angola in 2005. The present west African strain of ebola virus appears to be a variant of ZEBOV. The diseases caused by Ebola and Marburg viruses were earlier called as Ebola hemorrhagic fever (EHF) and Marburg hemorrhagic fever (MHF) but are now known as Ebola virus disease (EVD) and Marburg virus disease (MVD). A few confirmed ebola virus infections with some fatal cases have more recently been reported in August 2014 in an isolated region of DRC and this apparently appears to be a strain different from the present west African strain which is causing an unprecedented major outbreak of EVD.

EVD is essentially a zoonotic infection. The human epidemics are initiated by direct or indirect contact with nonhuman primates

(NHPs) like monkeys, gorillas or chimpanzees. In other parts of Africa where NHPs are rare, the disease may be acquired through contact with different species of frugivorous bats which are generally considered to be natural reservoirs of ebola virus. Bats do not themselves suffer from ebola virus infection but shed the virus in their saliva. Partially eaten fruits by bats if consumed by primates including humans can result in infection. Epidemics have been caused by direct exposure to bats [7]. Consuming uncooked, undercooked or smoked meat of NHPs or bats or the so called bush meat can be the source of infection. Large epidemics of EVD have been recorded in DRC and Uganda during the last few years [7,10]. Once the infection occurs in humans due to handling or consumption of bush meat, the virus spreads in the community through direct or indirect contact with blood and body fluids of the infected person or the deceased. After an incubation period of 2 to 21 days, the initial signs and symptoms like fatigue, fever, headache, muscle/joint pains and loss of appetite usually appear. Hemorrhagic rash, redness of eyes and bleeding from different orifices of the body including mouth, nose, ears, vagina and rectum are the common manifestations. The patient may pass blood in the vomit and sputum. The virus damages the internal lining cells of the blood vessels and leads to platelet dysfunction and profuse bleeding. This results in multiple organ malfunction, hypovolemic shock and death within 8 to 10 days. Super added bacterial and fungal infections may further account for increased morbidity and mortality. Ebola virus does not spread through air and is easily killed by soap and other standard disinfectants. Therefore, the chances of large epidemics or a pandemic are remote, though the virus has the potential to spread globally through infected individuals if quarantine measures are not strictly followed. Patients of EVD are not infectious during the incubation period but the virus may be present in semen even up to 7 weeks even after recovery. Therefore, the infection may be sexually transmitted by the convalescing patients.

The diagnosis of EVD depends on patient history and the clinical signs and symptoms, but the disease has to be differentiated from various other causes of hemorrhagic fevers including dengue fever and Lassa fever. The laboratory diagnosis is attempted only at specialized centers as the virus is labeled as Biosafety level 4. Immunofluorescent tests, ELISA tests, Electron microscopy, Virus culture and the RT-PCR are useful in the laboratory diagnosis of EVD. Since the virus has a close genetic relationship with *Rhabdoviridae* and *Paramyxoviridae* families, the results of the serological tests should be carefully interpreted and evaluated. The RT-PCR is a promising test in the rapid diagnosis of EVD from the early period of the disease to the early recovery stage. EVD is largely treated with intensive supportive and symptomatic measures. Ribavirin and interferon are ineffective. Blood transfusion, correction of the fluid and electrolyte imbalance through oral and IV fluids, administration of antipyretics, antibiotics and or antifungal drugs are the mainstay of the therapy. Administration of convalescent sera (taken from patients recovering from EVD) may be able to neutralize the virus as it has been found to be beneficial in a limited number of patients. Similarly well evaluated blood transfusion from convalescing patients may be equally useful. Presently no antiviral drugs or vaccines are formally approved by FDA for the treatment of EVD. However, there are many vaccines and antiviral drugs which are currently in different trial phases and it is hoped that an effective vaccine for the protection of contacts and the health care staff attending/treating patients of EVD is on the anvil and may be available by late 2015 or early 2016. The mutations in the viral genome may be a stumbling block in the development of an effective vaccine. Currently an experimental ebola virus vaccine is being tried in

humans. Needless to mention that about 10 to 15% of the medical and paramedical staff dedicated to the care of EVD patients have acquired the infection in different outbreaks with fatal outcome in many of them. It is pertinent to mention here that handling the ebola virus can be quite risky as five well experienced research authors/ scientists lost their lives while working with the present west African strain. It is well established that the present strain has mutated several times over the last few months. Two experimental drugs ZMapp and TKM-Ebola have been allowed by the FDA under special provisions for the treatment of EVD and some patients have shown encouraging results. ZMapp is a mixture of three humanized monoclonal antibodies and TKM-Ebola is an RNA interference drug. The scarcity and non-availability of these two drugs have apparently sparked some controversy in west Africa despite the fact that it is too early to predict the safety and efficacy of these antiviral agents.

The epidemiology of EVD is complex and requires thorough surveillance of the various factors operating in the ecosystem in the African endemic areas. EVD is a containable and a preventable disease if early appropriate measures are undertaken at personal, community and health care system levels. Prompt recognition, diagnosis, isolation and quarantine measures should be ensured. Clinical samples should be collected and shipped with due care. Barrier nursing and the use of masks, gloves, gowns and goggles should be encouraged together with the hand washing practice. All standard infection control measures as recommended by CDC, WHO and other international health authorities should be meticulously followed. Avoid all direct and indirect contact with blood, body fluids and other tissues of the ebola patients or the cadavers. No uncooked, undercooked or smoked meat of NHPs and bats should be consumed. All partially eaten fruits by the bats should be avoided. Laundry items of EVD patients should be collected, transported and washed/disinfected with utmost care. Aerosol generating procedures should be minimized. Social rituals (ministered by family members, relatives and friends) like cleaning the cadaver, cutting nails/hair and removal of clothes should be discouraged. The staff involved in embalming should follow the standard protocol not to come in contact with blood and body fluids of the deceased. While some airlines have suspended flights to west Africa, some countries have closed their borders and imposed Visa restrictions as precautionary measures. All non-essential travels to the affected areas should be avoided. The people returning from ebola affected areas and the contacts of the ebola patients should be monitored for signs and symptoms of the disease for three weeks and should seek medical care immediately if required.

Although significant international medical and financial help is being offered to the impoverished west African countries to help combat the present outbreak crisis, this may be too meager as EVD is furiously expanding its horizons given the fact that 40 % of the reported infections have occurred only during the last three weeks of August 2014. With the fragile basic health infrastructure and the lack of knowledge of mode of spread of the disease in the general west African public, it may take months to overcome the present epidemic even with all sincere efforts by various local and international missionaries. The social rituals, superstitions and unfounded rigid beliefs of the west African people are also major impediments in the control of the present epidemic of EVD. Needless to mention that the people in west Africa often rely more on treatment given by the traditional healers or quacks. As EVD has repeatedly been threatening many African countries ever since 1994, a clear ebola control strategy with practical implementation should be enforced both during epidemic and non-epidemic situations. The present epidemic of EVD

should be taken even more seriously than the major disasters like tsunami/earthquakes or epidemics like SARS, H1N1 and MERS-CoV. Even if we are successful in containing the present epidemic in the coming months, the devastation it has caused is certainly going to have significant long lasting economical, social and political impacts in the affected west African countries. This may have indirect economic repercussions on some other nations as well.

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