Review on Current Status of Ebola Virus Disease and its Zoonotic Significance in Africa

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Abstract: Ebola virus disease is one of the world's most virulent zoonotic diseases with a case fatality rate that can reach up to 90%. The current Ebola virus disease outbreak has reached five countries in West Africa, with over 14, 000 people have been infected and more than 5, 000 people have died in the affected countries up to 09 November 2014. The outbreak is the first in. An outbreak of Ebola virus disease has been ongoing, most persistent ever documented in West Africa since March 2014. Three countries (Guinea, Liberia and Sierra Leone) continue to report confirmed cases of Ebola virus disease (EVD) and has ended in Nigeria and Senegal, after having infected 20 people in Nigeria and one in Senegal. The outbreak is exacerbating in the affected countries face severe deficiencies of human resources, commodities, information and financing. Despite the fact that no detection of the virus had been discovered in Ethiopia so far, all the necessary precautions should be made to prevent the virus from entering the country. Ethiopian Airlines has been informing passengers on ways to reduce risking exposure and preventing the spread of the disease for those traveling to and from affected countries. Ebola virus disease caused by members of the genera Ebola virus, in the family *Filoviridae*. The exact origin, locations and natural reservoir of Ebola virus remain unclear. People can be exposed to Ebola virus from direct contact with the blood and/or secretions of an infected person. Hunting and butchering of wildlife (great apes and fruit bats) has been identified in previous outbreaks as a potential source of infection. The onset of Ebola virus disease is sudden and early symptoms include flu-like illness, fever, myalgia, fatigue, headache and sore throat, followed by abdominal pain, nausea, vomiting and diarrhea. Patients in the final stage of disease die in the clinical picture of massive bleeding, metabolic disturbances, severe dehydration, diffuse coagulopathy, tachypnea, anuria, hypovolemic shock and multi-organ failure. Ebola virus infections can be diagnosed by detecting antigens with an antigen-capture ELISA and by detecting viral RNA with RT-PCR. Electron microscopy can identify virus particles. Standard treatment currently consists of supportive therapy, including maintenance of blood volume and electrolyte balance, as well as analgesics and standard nursing care. No specific treatment has been demonstrated yet to be safe and effective in humans; however, experimental drugs, vaccines and monoclonal antibodies to filovirus have been tested in animals, with varying degrees of success in nonhuman primates. To prevent infection from animals that might be infected but have not yet developed obvious clinical signs, good personal hygiene should be used when handling and preparing meat and the meat should be thoroughly cooked. Human epidemics can be stopped by isolating patients in facilities with barrier nursing procedures and strict infection control measures. Healthcare workers should use the personal protective equipment currently recommended by experts to prevent exposure to blood and body fluids. Burial practices should avoid all contact with the body or fomites. During convalescence, the possibility of exposure during breastfeeding or sexual intercourse should be considered.

Key words: Ebola Virus Disease · Zoonotic virulent disease · Africa · Current Status

INTRODUCTION

Ebola viruses is incompletely understood pathogens that cause severe, often fatal, illnesses in humans and non-human primates (monkeys, gorillas and chimpanzees) that have appeared sporadically since its initial recognition in 1976[1]. The disease has been known as Ebola hemorrhagic fevers, after the most dramatic symptoms in severe cases. The names "Ebola virus disease" (EVD) is now preferred by the World Health

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Organization (WHO) and some other groups [2,3]. The disease has high fatality rates and has caused more than 1,500 deaths in parts of Africa since the 1970s. Ebola virus is named for the Ebola River in the Democratic Republic of the Congo, where the virus was first identified in 1976. The animal hosts of the viruses remain largely unknown, but evidence points to the role of fruit bats as possible natural hosts (called reservoir hosts) of Ebola virus [4].

The current Ebola virus disease outbreak has reached five countries in West Africa, with 14,000 documented cases and over 5,000 deaths up to November 2014 [5]. A separate, unrelated Ebola outbreak has also been reported in the Democratic Republic of the Congo. Ebola virus disease is one of the world's most zoonotic virulent diseases with a case fatality rate that can reach up to 90%. Ebola virus disease occurs primarily in remote areas of Central and West Africa. There have been 24 documented outbreaks since 1976, each averaging ~100 cases and a case fatality rate (CFR) of 66%. Twenty six million people, including 10.3 million children live in the areas affected by Ebola [6].

Etiology: Ebola Virus disease is caused by members of the genera Ebola virus, in the family *Filoviridae*. The names of these viruses have undergone several taxonomic changes since they were first discovered, including new changes officially accepted in 2013. Currently, the genus Ebola virus contains five recognized viral species: Zaire ebolavirus, Sudan ebolavirus, Taï Forest ebolavirus (formerly Cote d'Ivoire ebolavirus), Reston ebolavirus and Bundibugyo ebolavirus [7]. The common name for the single virus in each of these species is Ebola virus (formerly Zaire ebolavirus), Sudan virus (formerly Sudan ebolavirus), Tai Forest virus (formerly Cote d'Ivoire ebolavirus), Reston virus (formerly Reston ebolavirus) and Bundibugyo virus. Marburg virus contains a single species [3,8].

Distribution: The known geographic range of primary Filovirus infection is in tropical Africa with the exception of Reston Ebola virus, which occurs in Philippines. The fact that the Ebola virus subtypes that have caused human disease episodes have been different from each other makes it clear that a common source transmission chain extending across sub-Saharan Africa is not the case rather distinct virus subtypes from each site of human disease episodes have been responsible [1].

Previous outbreaks were confined to rural and forested areas, whereas the current outbreak is spreading in rural and urban settings alike. Responders are struggling to isolate cases and contain the outbreak in densely populated urban areas that lack sufficient access to clean water and sanitation and face severe shortages of health workers and clinics. There is increasing frequency of outbreaks in sub-Saharan Africa of which significant ongoing outbreaks in wild (endangered) non-human primate species (chimpanzees) [9]. The exact origin, locations and natural habitat (known as the "natural reservoir") of Ebola virus remain unknown [2].

However, on the basis of available evidence and the nature of similar viruses, researchers believe that the virus is zoonotic with four of the five subtypes occurring in an animal host native to Africa. A similar host, most likely in the Philippines, is probably associated with the Ebola-Reston subtype, which was isolated from infected monkeys that were imported to the United States and Italy from the Philippines. The virus is not known to be native to other continents, such as North America. Confirmed cases of Ebola virus disease has been reported in the Democratic Republic of the Congo, Gabon, Sudan, the Ivory Coast and Uganda. Ebola virus disease typically appears in sporadic outbreaks, usually spread within a health-care setting. It is likely that sporadic, isolated cases occur as well, but go unrecognized [2,7].

Transmission: How filovirus is transmitted between bats, or transmitted from bats to other animals, is still uncertain. Although this virus can be found in bat tissues and blood, it typically seem to be absent from secretions or excretions such as oral fluids, urine and feces (although virus was found in the feces of one experimentally infected bat) and attempts to inoculate bats by exposing respiratory and oral mucus membranes to virus were unsuccessful. It is possible that virus shedding in secretions and excretions occurs intermittently, at very low levels and/or under certain physiological conditions. There is some evidence that transmission might occur when bats give birth. Filovirus emerges periodically in nonhuman primates or people after infection from an outside source [3,8,10].

Some Ebola virus might also be acquired directly from bats; however, humans often become ill after handling the carcasses of animals found in the forest, especially nonhuman primates and duikers. Blood, secretions and excretions and tissues from these animals may contain infectious virus. *Filovirus* has been reported to survive for some time in blood and tissues at room temperature and can be transmitted on fomites, particularly those contaminated by blood [3]. In incidental hosts, filovirus is thought to enter the body mainly through mucous

membranes and broken skin. Arthropod-borne transmission is theoretically possible, but most authors suggest it is unlikely. Once Ebola virus has infected humans, they can spread from person to person. Blood can contain large amounts of virus, contaminating the environment if patients hemorrhage. These viruses are also found in many secretions and excretions that are not visibly contaminated with blood, including saliva, tears, breast milk, semen and feces. Urine may be a source of virus, but Zaire ebolavirus was absent from patients' urine during one outbreak. Aerosol transmission has been reported in some experimentally infected nonhuman primates, although virus does not seem to spread readily between cages in other studies [5,11].

After the first case-patient in an outbreak setting is infected, the virus can be transmitted in several ways. People can be exposed to Ebola virus from direct contact with the blood and/or secretions of an infected person [12]. Thus, the virus is often spread through families and friends because they come in close contact with such secretions when caring for infected persons. People can also be exposed to Ebola virus through contact with objects, such as needles, that have been contaminated with infected secretions [5]. Hunting and butchering of wildlife (great apes and fruit bats) has been identified in previous outbreaks as a potential source of infection. Bats remain the most likely, but still unconfirmed, reservoir host for Ebola viruses. Nosocomial transmission also possible [3,7,12].

Clinical Signs: The onset of Ebola virus disease is sudden and early symptoms include flu-like illness, fever, myalgia, fatigue, headache and sore throat. The next stage of the disease is characterized by symptoms and clinical manifestations from several organ systems. Symptoms can be gastrointestinal (vomiting, diarrhea, anorexia and abdominal pain), neurological (headaches, confusion), vascular (conjunctival/pharyngeal injections), cutaneous (maculopapular rash) and respiratory (cough, chest pain, shortness of breath) and can include complete exhaustion (prostration). During the first week, patients often deteriorate suddenly, while diarrhea and vomiting are getting worse. All of these symptoms correspond to the prodromal phase of Ebola virus disease. After one week, hemorrhagic manifestations can appear in more than half of the patients (bloody diarrhea, nosebleeds, hematemesis, petechiae, ecchymosis and puncture bleedings). Some patients develop profuse internal and external hemorrhages and disseminated intravascular coagulation. Patients in the final stage of disease die in the clinical picture of massive bleeding, metabolic disturbances, severe dehydration, diffuse coagulopathy, tachypnea, anuria, hypovolemic shock and multi-organ failure. Pregnant women may abort [3,8,12,13].

Diagnostic Tests: Filovirus infections can be diagnosed by detecting antigens with an antigen-capture ELISA and by detecting viral RNA with reverse transcription polymerase chain reaction (RT-PCR). Electron microscopy can identify virus particles, which have a distinctive, filamentous pleomorphic, appearance, in tissues. In primates, filoviruses occur in high concentrations in the liver, spleen, lungs, lymph nodes and skin. Liver, spleen, muscle and skin have been taken from wild animal carcasses in good condition for surveillance by RT-PCR. This test can sometimes detect Ebola virus RNA in the bones of decomposed carcasses. In bats, filoviruses have been found in tissues such as the liver and spleen and sometimes in the blood. Serological tests include indirect immunofluorescence (IFA) and ELISAs, but neutralization tests are unreliable for filoviruses. Cross-reactions can occur. Immunoblotting may be used in research [3, 5, 8,10,14].

Treatment: Standard treatment currently consists of supportive therapy, including maintenance of blood volume and electrolyte balance, as well as analgesics and standard nursing care. No specific treatment has been demonstrated yet to be safe and effective in humans; however, experimental drugs, vaccines and monoclonal antibodies to filoviruses have been tested in animals, with varying degrees of success in nonhuman primates. These experimental treatments are diverse and may be aimed at inhibiting virus replication and/or entry into cells, treating clotting abnormalities or sepsis, or boosting immune responses. Most experimental treatments have been tested very early in the incubation period, but some were promising when started up to 2 days after exposure, or even after early clinical signs (e.g., mild elevation in temperature) developed. A few drugs have advanced to human phase I clinical trials, which are the initial tests to determine whether agents appear to be safe for human use. When supplies are available, some experimental treatments have been used in humans on a compassionate basis [3, 15].

Control and Prevention
Control: Disease reporting- international health regulations require that nations report acute hemorrhagic fever syndromes immediately to World Health

Organization (WHO, 2014), without waiting for the causative agent to be identified. Suspected human cases of Ebola fever should be reported immediately to the nation's public health service, to prevent transmission and aid in case management and diagnosis [3, 14].

Prevention: In Africa, Ebola virus infections are often linked to exposure to wild animal tissues during butchering. Because the full host range may not be known, all sick and dead wild animals should be avoided (including for use as food). To prevent infection from animals that might be infected but have not yet developed obvious clinical signs, good personal hygiene should be used when handling and preparing meat and the meat should be thoroughly cooked. Surveillance for deaths and illness in wild animals may provide an early warning to prevent human epidemics, but such deaths have not been seen in all human outbreaks [3].

Infections have been linked to exposure to caves, mines and cave-dwelling bats, but the means of transmission from bats to humans is still unknown. If contact is unavoidable (e.g., occupational exposure), personal protective equipment and good hygiene should be used. Some caves have been closed after human cases were recognized. Human epidemics can be stopped by isolating patients in facilities with barrier nursing procedures and strict infection control measures. Healthcare workers should use the personal protective equipment currently recommended by experts (gloves, gowns, masks, eye protection and other equipment) to prevent exposure to blood and body fluids [16].

Burial practices should avoid all contact with the body or fomites. During convalescence, the possibility of exposure during breastfeeding or sexual intercourse should be considered. Ebola viruses have been found in milk 15 days after the onset of illness (although the maximum period of shedding is unknown) and in semen for much longer. Sexual abstinence has been recommended for at least three months after recovery. As a precaution, tissues from infected animals should not be eaten or handled [17].

Current Status and Outbreaks in Africa of Ebola Virus Disease: Although the Ebola virus disease was new to science in the 1960s, it may have existed in nature for thousands of years. The disease may have occasionally struck humans who came in contact with the still largely unknown natural hosts (called reservoir hosts). Outbreaks in human populations likely remained local and isolated because of the need for direct physical contact to spread

the diseases, as well as rapid and high mortality rates. The general similarity of some symptoms to other types of endemic hemorrhagic fevers or acute illnesses also meant that cases of Ebola might not be recognized as specific diseases [18].

The first recognition of the Marburg virus came in 1967, when 31 cases of hemorrhagic fever, with seven deaths, occurred among laboratory workers in Germany and Yugoslavia who were processing kidneys taken from African green monkeys (*Cercopithecus aethiops*) that had been imported from Uganda. A new virus was isolated from patients and monkeys; it was named Marburg virus, now the prototype of the family Filoviridae or filoviruses. Two epidemics of hemorrhagic fever occurred, one in Zaire (now the Democratic Republic of the Congo), the other in Sudan. Altogether there were more than 550 cases and 430 deaths. A virus with a physical shape identical to the Marburg virus but with distinct antigens was isolated. It was named Ebola virus. Later, the viruses from Zaire and Sudan were found to be genetically distinct and are now designated Ebola virus Zaire and Ebola virus Sudan. The two viruses differ in their pathogenicity also, with the Zaire virus causing death in about 80 to 90 percent of infected persons and the Sudan virus in about 50 percent. The Ebola virus Côte d'Ivoire was discovered when a single human case was identified in Côte d'Ivoire. The genetically distinct virus was isolated from a person who had examined the dead body of a wild chimpanzee from a troop of chimps that had suffered high mortality. Since 1976 there have been many more episodes of Ebola hemorrhagic fever, representing an ever increasing geographic range within Africa [4,8, 19].

In 1989 and 1990 monkeys (*Macaca fascicularis*) imported from the Philippines into a facility for the import and sale of laboratory animals in Reston, Virginia, were found to have been infected with another new virus, now called Ebola virus Reston. Infected monkeys at the facility became ill and many died. Four animal caretakers were infected but there was no clinically apparent disease. This virus reappeared in imported monkeys in Italy in 1992 and Texas in 1996. Cases of Ebola and Marburg hemorrhagic fevers have been increasing in Africa in recent years, occurring as large and small outbreaks, involving an ever-expanding geographic range. Between 1967 and the early 1990s several smaller outbreaks caused by these viruses were recorded in various parts of western and central Africa. From the mid-1990s onward, the viruses have become more common and widespread, usually in settings where there has been environmental degradation

of previously uninhabited areas, such as may happen with gold mining. People may have no immunity to new microbes contacted in unfamiliar ecosystems [15].

Ebola virus has also emerged as a deadly threat to gorilla populations. Researchers reported that more than 5,000 gorillas in the Republic of Congo and in Gabon died from Ebola virus disease just between 2002 and 2004. Similarly, there have been reports of large numbers of chimpanzees dying of Ebola virus disease in the same areas as the gorilla deaths. The disease has apparently been spread by contact, even between territorial social groups. The loss of such large numbers of gorillas and chimpanzees adds to the extinction threat for these animals [4].

An outbreak of Ebola virus disease has been ongoing in West Africa since March 2014. It is the largest outbreak known to date [10]. As of 10 September 2014, three countries (Guinea, Liberia and Sierra Leone) continue to report confirmed cases of Ebola virus disease (EVD) and has ended in Nigeria and Senegal, after having infected 20 people in Nigeria and one in Senegal. New confirmed cases have been reported in the following localities of the three countries: Guinea (Conakry, Guékedou, Macenta, Siguri, Forécariah and Kérouane); Liberia (Grand Cape Mount and Lofa) and Sierra Leone (Kenema, Port Loko, Western Area Urban, Western Area Rural, Kono, Tonkolili and Bombali). Laboratory results for the new suspected cases in Democratic Republic of the Congo are expected today [20].

Risk Factors and Constraints in Affected Countries
Financing: Per capita health spending in Guinea, Liberia and Sierra Leone has been relatively low, contributing to poor conditions of publicly-funded health facilities. Health workers and other government personnel often experience delays in compensation and benefits, contributing to absenteeism and human worker shortages. As the Ebola outbreak intensified, some health workers abandoned their posts, citing not only safety concerns (from lack of protective equipment) but also frustration over not receiving salaries. Several local staff at Ebola treatment units in Liberia had reportedly not been paid for three months. Fourteen donors, including the United States, have since begun to offer financial aid to Liberia to support payment of health workers salaries and other financial incentives [21].

Human Resources: Due to severe shortages of health workers and clinics, the majority of people infected with Ebola in Liberia are without access to medical care and treatment. Inadequate access to health personnel and facilities is also a problem in Sierra Leone and Guinea. Human resource constraints and concerns about conditions in health centers are prompting people to care for the ill on their own, facilitating the spread of the virus. The shortage of medics and health facilities also means that people needing care for non-EVD related issues have nowhere to go [5].

Commodities: Shortages of protective gear are associated with EVD cases among health workers and may allow EVD to be spread within health facilities. The affected countries have limited supplies of appropriate protective equipment and not all health and support personnel who interact with the public have access to such equipment. Due to resource constraints, the protective equipment is primarily provided to healthcare workers in Ebola treatment centers, leaving health workers who operate among the general population at risk of contracting and spreading the disease (and other infectious diseases) should they encounter an undiagnosed EVD case. Health providers also lack sufficient supplies of antibiotics and safe blood to treat Ebola. The price of disinfectants and medicine has reportedly doubled, as people attempt to protect themselves and self-medicate in light of health system deficiencies [22].

Table 1: Summary data from the countries from March to September 2014

Countries	New cases/deaths		Cumulative number		Health Care Workers	
	Cases	Deaths	Cases	Deaths	Cases	Deaths
Guinea	22	2	899	568	57	28
Liberia	59	46	2407	1296	169	82
Nigeria	0	0	21	8	11	5
Sierra Leone	42	3	1478	536	56	30
Senegal	0	0	1	0	0	0
DR Congo	3	1	66	37	9	7
Total	126	52	4872	2445	302	152

Sources: (WHO, 2014)

Information: Awareness about preventing EVD infection has improved, but due to poverty, infrastructural deficiencies (e.g. clean water and sanitation) and health system constraints, many people lack means to avoid infection. Before Ebola hit, hunger was already a problem in the affected countries, particularly in rural areas. Consumption of wild animals is common practice, particularly in areas with high food insecurity. Health officials have been expanding efforts to inform the public about the risks associated with eating wild animals, including fruit bats and other animals that might carry EVD. Without sufficient access to food, hunger often compels people to continue hunting and eating the animals despite the risks [21].

Disease Status and Measures to Prevent Ebola Virus Disease in Ethiopia: Medium risk countries are listed such as Nigeria, Kenya and Ethiopia. Note that some of these countries like Kenya and Ethiopia have no Ebola yet, but are mentioned here because most people travelling from West Africa to South Africa travel via these countries [23]. Following the outbreak in Liberia, Guinea and Sierra Leone, Ebola was declared to be a public health emergency in West Africa by the WHO Director General in July 2014 and countries with close travel and contact with affected countries were advised to strengthen preparedness and surveillance [8]. The FMoH organized the orientation workshop taking heed of this declaration and also considering the fact that Ethiopian Airlines has flights to and from the affected countries. Strict monitoring at Ethiopia's borders in cooperation with regional states is underway to prevent the spread of the Ebola Virus into the country, the Minister of Health announced. Deputy Prime Minister Ethiopia stated that despite the fact that no detection of the virus had been discovered in Ethiopia so far, all the necessary precautions should be made to prevent the virus from entering the country. He also stated that the public's health is top priority.

According to Federal Ministry of Health (FMoH)[24] of Ethiopia, the national committee has enabled the ministry to work in collaboration with different stakeholders. He also stated that extensive work in creating awareness about the disease is being carried out. The Woreda health center care givers are receiving training to commence a 24 hour a day monitoring at international borders. The spread of the disease in Nigeria is reportedly low and Ethiopian Airlines will continue to fly there with extreme precautions. It was stated that the

decision by Kenya Airways to halt all flights to Guinea, Liberia and Sierra Leon has lowered the fear of the spread of the disease to East Africa.

According to reports, Ethiopian Airlines is also taking precautionary measures against the spread of Ebola. The airline has been informing passengers on ways to reduce risking exposure and preventing the spread of the disease for those traveling to and from affected countries. The airline also requires passengers to fill in surveillance forms before boarding for traceability purposes; and precautionary testing is being conducted by health officials on passengers before boarding and after arriving. Recently, the World Health Organization has stated that air travel is low risk for Ebola transmission and air transport hubs are not high risk for the spread of Ebola [25].

Addis Ababa 6 August 2014 - A half-day orientation on Ebola virus disease outbreak preparedness and response organized by the Federal Ministry of Health (FMoH) took place in Addis Ababa. The orientation workshop was organized to orient health workers on the Ebola virus disease surveillance (case detection and reporting), risk factors, clinical signs and symptoms and precautions to be taken for infection prevention. More than 200 health workers from government and private hospitals, NGOs, health centers, health bureaus and sub-cities in Addis Ababa and Ethiopian Airlines Clinic attended the orientation. Also present were representatives from the World Health Organization (WHO), the US Center for Disease Control and Prevention (CDC) and Japan Embassy of Ethiopia [26]. The country also assigned one hospital and one clinic for those suspected Ebola virus disease in the quarantine.

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