EBOLA VIRUS DISEASE

Abstract

The largest ever-recorded Ebola Virus Disease (EVD) epidemic continues to ravage West Africa. Ebola virus (EV) is a non-segmented single-stranded RNA virus that has five strains. The 2014-2015 outbreak began in Guinea, West Africa in December 2013, and, as of 12 November 2015, the aggregate number of cases (suspected, probable, or confirmed) exceeded 28,630, including over 11,300 deaths (World Health Organization [WHO], 2015). The virus is transmitted from the infected individuals to others by contact with skin, blood, saliva, and other body fluids. The early symptoms include fever, anorexia, myalgias, and acute headaches. A number of international organizations have deployed massive relief campaigns in West Africa. Central elements of the plan involve contact tracing, follow-up, increase community awareness, and social mobilization. As of September 2015, the World Bank Group has invested a total of $1.62 billion into the anti-Ebola efforts in West Africa. The USA allocated around $1.4 billion of financial aid to fight this disease.

The ongoing outbreak of Ebola is broke all the records with the total number of fatal cases exceeding 11,300. The international health community has been forced to respond immediately, and medical professionals work indefatigably to aid suffering communities. The virus contains single-stranded RNA, and four of the five known species induce disease in humans. The present-day epidemic, the first to strike in West Africa, is caused by the Zaire strain, which has previously been reported to have the mortality rate of 78%. This research paper will focus on the key features of epidemiology, clinical manifestation, diagnosis, and current treatment tactics of EVD, as well as discuss measures of disease containment and prevention.

History of the Disease

The scientists discovered filovirus in 1967, when the incautious transportation of diseased monkeys from Uganda resulted in a massive epidemic of acute illness among the medical plant employees in the German city Marburg. The causative agent, called the Marburg virus, provoked a series of epidemics in Africa, the latest of which occurred in Uganda in 2014.

Ebola virus, the second of the filoviridae genera, was first encountered in 1976 when two outbreaks exploded in Sudan and Zaire. Epidemics of EVD have been geographically limited to Sub-Saharan Africa. In 1995, an outbreak induced by the Zaire strain diseased several hundred people in Democratic Republic of the Congo, while over four hundred were exposed to the Sudan species five years later in the Ugandan region of Gulu. The current outbreak, caused by the Zaire virus, is the first to strike in West Africa and considerably exceeds all of the previous ones in magnitude and duration.

Causative Factor

Ebola virus (EV) is a non-segmented single-stranded RNA virus, which is similar to paramyxoviruses and rhabdoviruses in replication mechanisms and genome organization. It belongs to *Filoviridae*. The EV is enveloped, threadlike, and filamentous, and has a nucleocapsid and extensive branching. Typically, the virus reaches 80 nm in diameter and 1000-1200 nm in length. Formerly, EV and Marburg virus belonged to a group of haemorrhagic fever viruses, since they were presented with impaired coagulation, bleeding, and shock. Nonetheless, the term *haemorrhagic fever* is no longer associated with EVD as the percentage of patients who actually develop acute bleeding is insignificant, and haemorrhage typically occurs in the terminal stages of illness.

EV has five strains, namely Zaire, Sudan, Bundibugyo, Ivory Coast, and Reston. The next four cause a disease in humans:

- First discovered in 1976, the Zaire virus has become the cause of numerous severe epidemics in Central African countries. Case-fatality rates range from 54 to 88 percent. Zaire strain is a causative factor of the outbreak in West Africa.
- The Sudan strain caused a number of outbreaks in Sudan and Uganda. Nearly half of the patients died in the 2000 Uganda epidemic.
- The Bundibugyo species was found in 2007. It caused an outbreak in Uganda with a mortality rate of nearly 30 percent. This subtype resembles the Ivory Coast strain.
- The Ivory Coast virus has only been proven to induce illness in one individual, and that person survived. Presumably, the infection occurred when the zoologist operated on a dead chimpanzee found

in the Tai Forest, where striking reductions in the ape population had been identified.

The Reston virus, the last of the Ebola strains, is notably different from the four others since it seemingly circulates within an animal reservoir on the Philippine islands and has never been detected in Africa. This strain was brought to attention after an epidemic of fatal infection in macaques transported to the U.S. in 1989. Outbreaks among primates in the quarantine zones in the U. S. and Europe reoccurred until the Philippine animal importer terminated operations. No cases of disease were registered among the caretaking personnel. However, some of the members demonstrated signs of seroconversion.

In 2008, an epidemic of severe illness affecting pigs occurred in the Philippines. The studies revealed both arterivirus and Reston virus in the infected animals. Serologic investigations identified IgG antibodies in some of the pig farmers. However, they never developed acute symptoms.

Transmission

Outbreaks of EVD are believed to start when a person is exposed to the meat or bodily fluids of a diseased animal. Once an individual becomes sick, the virus is transmitted to those contacting with the patient's skin, blood, saliva, and other body fluids. Laboratory studies on apes demonstrated that animals could get EV infection via droplet inoculation of virions into the eyes or mouth, implying that humans could become infected transferring viral agents on contaminated hands.

Methods of Containment

In August 2014, WHO designed a detailed action plan, providing thorough instruction on how to curb the epidemic and contain the disease. Central elements of the plan involve contact tracing, follow-up, increasing community awareness, and social mobilization. The poor functioning of healthcare systems in African countries is believed to be among the key reasons that impede taking adequate measures against the spread of Ebola.

Contact tracing is central for the prevention of the disease. The method includes efficient public surveillance so that the likely carriers of Ebola can be registered and diagnosed in shortest period, with subsequent detection of individuals who had contacted the source and observing them for 21 days.

Epidemiology of the Current Epidemic

The ongoing EVD outbreak began in Guinea, West Africa in December 2013. The epidemic is believed to have begun from a two-year-old child who has been hospitalized with fever, black stool, and vomiting. The outbreak rapidly expended to Sierra Leone, Liberia, Nigeria, Mali, and Senegal. Sequence determination signified that the outbreak has resulted from maintained person-to-person transmission, with no contribution from animal reservoirs.

The size of the outbreak, specifically in Sierra Leone and Liberia, has long been underestimated for the most part, because many individuals infected with Ebola virus did not submit themselves to the hospitals. As of 12 November 2015, the aggregate number of cases (suspected, probable, or confirmed) equaled 28,635, including over 11,300 deaths. The numbers include the minimum of 830 infected medical workers, nearly 60 percent of which have died. In Nigeria, Mali, and Senegal, where transmission has been

localized, the outbreak is considered to have been eradicated.

Four cases of EVD have been registered in the US. The first case was identified on September 30, 2014. The individual died on October 7. In December 2014, EV was extracted from a patient in the UK.

Symptoms

Incubation period ranges between three and eight days, however, can last somewhat longer in repeated cases. In rare cases, incubation period may even reach 21 days. Sudden onset of clinical signs is typical of EVD. The early symptoms include fever, anorexia, myalgias, and acute headaches. Gastrointestinal syndrome (diarrhea, abdominal pain, nausea, and vomiting) develops soon. Signs of mucous membrane involvement include dysphagia and conjunctivitis, bleeding from the GI tract has been observed in 40-50 percent of patients. A rash follows in approximately 15 percent of cases. Terminally ill individuals are exhausted, blunt, tachypnoic, anuric, and often in shock. Ophthalmic complications were seen in three of twenty patients that survived in the 1995 Ebola outbreak in DRC. Photophobia, oculodynia, blurred vision, and excessive lacrimation were the common complaints. Some of the remote symptoms include hearing loss, orchitis, amenorrhea, and parotitis.

Diagnosis

Diagnosing Ebola on early stages is problematic as the symptoms in the first days are nonspecific. EV is only found in blood after many of the symptoms appear. Leukopenia, thrombocytopenia, lymphopenia occur early after virus reaches the blood stream. Neutrophilia follows soon and aminotransferases

increase. Creatinine elevation appears with anuria. Tachypnea in fatally ill patients often results in metabolic acidosis. Apart from the basic blood test, some of the applicable laboratory arrays include the following.

Virus Isolation and Molecular Methods

Isolation of the virus is performed using either tissue cultures or RT-PCR assay. Virus isolation in tissue culture is a dangerous procedure and can only be accomplished safely in a restricted number of leading laboratories in the world.

RT-PCR was effectively applied for virus detection in the current epidemic as well as in some previous outbreaks. The EZ1 Real-time RT-PCR is among the most efficient methods to confirm the presence of the EV. Only the US Department of Defense, which chooses laboratories that will cope with hazardous samples, can authorize the assay. The assay enables individuals suspected with having infection to acquire the results of their tests few hours after the samples are taken. The method utilizes a dual-labeled FRET probe with a quencher and reporter dye. High sensibility and speed of this assay have placed them in the forefront of diagnostics during several major disease outbreaks such as the 2009 H1N1 pandemic.

Serological Testing

The indirect fluorescence antibody test (IFAT) rests on false-positive results. Worries over the specificity and sensitivity of this assay has led to the development of confirmatory tests. IgM and IG enzyme-linked immunosorbent assay (ELISA) tests may contribute to the diagnosis of EVD in individuals who have developed immune response. Both of the ELISA tests

have proven to be sensitive and specific.

During IgM-capture ELISA test, *Zaire virus* antigens incubated in Vero E6 cells are used to detect IgM antibodies to this species. In experimental apes, positive results are obtained within 6 days of getting infected. However, they are negative after longer periods. Such qualities suggest that the test should be used only in the early stages of the EVD.

IgG-capture ELISA with detergent-extracted viral antigens effectively detects IgG anti-EV antibodies. The specificity is higher than in the IFA, and the results remain positive for extended periods. Therefore, this test is seemingly the most effective among the known serological methods.

Treatment options

Usually, treatment options in EVD patients are confined to supportive therapy and involve maintenance of intravascular volume, control of electrolytes, and proper nutrition. However, some newer therapies have been added recently. One of those is ZMAPP, which is a complex of three humanized monoclonal antibodies. After a series of positive experiences in primates, the remedy was tried on humans. The numbers are yet insufficient to estimate its efficacy.

Public Health Costs

As of September 2015, the World Bank Group has invested a total of $1.62 billion into the anti-Ebola efforts in West Africa. Most of the finances were received by the three most affected countries: Guinea ($260 million), Liberia ($385 million), and Sierra Leone ($318 million). The minimum of $1.17 billion

came from IDA, the World Bank Group's foundation for the least developed states, and approximately $450 million were donated by IFC to boost trade and improve employment in the Liberia, Sierra Leone, and Guinea. Additionally, the US allocated around $1.4 billion of financial aid to build 11 treatment centers in Liberia and 3000 troops have been deployed for relief efforts.

Required Educational Efforts

Instructional work should be carried out with all of the caregiving personnel, and the emphasis should be placed on the use of protective equipment as a primary measure against infection. CDS has elaborated the guidelines for medical laboratorians that are based on three fundamental principles:

- Healthcare workers delivering care for patients with Ebola undergo extensive training and display competency in performing infections control procedures.
- When working with PPE, skin should not be exposed.
- A senior manager must continuously monitor compliance to safety measures in a facility with Ebola patients.

Increasing the knowledge of modes of transmission and causative factors of infection among the population is also necessary. People must be aware of the risks of contacting with the infected persons and realize the importance of regular hand washing. To pursue this goal, a number of international organizations should engage and specially train local volunteers.

Conclusion

EVD has caused one of the most severe epidemics in the recent history, becoming the reason of over 11,300 deaths. Ebola virus, one of the *filoviridae genera*, causes the disease and is highly contagious. Most frequently, virus affects individuals through the contact with infected bodily fluids of the diseased patients. Early symptoms of EVD are not unique for the disease, and the condition is difficult to identify during the early stages. Modern diagnostic arsenal incorporates serological testing, virus isolation, and molecular methods. Treatment options are mainly limited to maintenance therapy, though, novel medications such ZMAPP are underway. Major efforts of international organizations are targeted at education of personnel and general population on ways of disease transmission and methods of prevention.