Past, Present and Future about Ebola Virus Diseases: An Updated Review

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ABSTRACT

Ebola virus is responsible for the Ebola virus diseases. The epidemic of Ebola hemorrhagic fever is a deadly disease of animal can also be transmitted to human and non-human primates. The virulence of Ebola virus involved in several immune evasion mechanisms that include an inhibition of type I interferon responsible for innate immunity, epitope masking, etc. recently Ebola virus is sexually transmitted which was reported in Liberia has associated with new clusters in regions previously declared Ebola-free. There is no appropriate antiviral vaccine or therapy is not available to work against EBOV infection in humans. However, supportive recovery practices are performed include high-fluid intake, ventilator support and broad-spectrum antibiotic therapy. The treatment and diagnosis is very important because these kind of dangerous viruses are possibly used for bio-weapons. The present review describes briefly about virology, epidemiology, pathophysiology, transmission, diagnosis and treatment of Ebola viral disease.

Key words: Ebola virus, Filovirus, RT-PCR, Drug, Vaccine Development.

INTRODUCTION

Ebola virus is Precarious corresponding to Ebola virus disease (EVD). Ebola first appeared in 1976 in two simultaneous outbreaks, in Nzara, Sudan, and in Yambuku, Democratic Republic of Congo. It has not been reported in humans in the Asia Pacific region as of 31 July 2012. However, with global traveling it is possible that outbreaks in Africa could result in the spread of the virus to Asia specifically in India. There are different species of the Ebola virus. Of these, the Reston ebola virus was first discovered in laboratories in Reston, Virginia, United States of America (USA) in 1989 after some quarantined, crab-eating macaque monkeys originating from the Philippines became ill and died. In 2008, a virus identified in pigs was found to be very similar to the virus identified in monkeys imported into the USA for research from the Philippines in 1989. The World Health Organization has declared a public health emergency of international concern and also called all nations for a coordinated international response to investigate, detect and manage Ebola cases.

Virology

Filoviruses (family Filoviridae) are enveloped, linear, Class V, (-) SS-RNA viruses belonging to the order Mononegavirales. Ebola and Marburg virus are the two genera of filoviruses that have been identified to cause severe disease in humans. Five Ebola virus species (Bundibugyo ebolavirus, Zaire ebolavirus, Sudan ebolavirus, Reston ebolavirus, Tai Forest (formerly Côte d’Ivoire ebolavirus) First four cause Ebola virus disease in humans and a fifth species has only caused disease in nonhuman primates. Virions of the EBOV genome are made with a core of single negative-sensed RNA, also contain proteins such as viral proteins 24, 30, 35 and 40, nucleoprotein,
L protein and glycoprotein (GP). The structural similarity of genome among the species brings a wide genetic divergence. In addition, phylogenetic analysis of GP gene sequences of EBOV confirmed that epidemic EBOV-Z strains shown close genetic relationships.[7]

**Ebola Outbreaks**

According to Ebola Situation Report In West African Countries more than 11,000 deaths and 28500 Suspected Cases are found. Recently there is no confirm victim found from Dec 2015 to 6 Jan 2016, due to migration It is spread in European countries, suspected cases found in Spain, Italy and United kingdom, the worldwide Suspected cases shown in Figure 2 (WHO 2016).

**Epidemiology**

The filovirus hemorrhagic fever was primarily recognized in Germany and Yugoslavia in 1967. The causative virus was named as Marburg virus.[9] Southern Sudan and Northern Zaire were affected with an epidemic of hemorrhagic fever was reported in 1976. In the name of Ebola River, located in the north western Democratic Republic of the Congo, an uncertain infectious agent was named as the Ebola virus. In 1994, the third Ebola virus species were found in the Tai forest where an ethnologist had performed the post-mortem examination on chimpanzee was living with other members of its species were dying due to EHF.[10] The Ebola virus had primarily identified in the area of the rain forests of Central Africa. In recent, it entered epidemically to the distant villages of Central and Western Africa. WHO, CDC (Center for Disease Control), and many international associations have updated the recent knowledge about EVD to students, travelers and clinicians. The high fatality rate (60-90%) of EVD outbreaks depends on the accessibility of appropriate medication, time of diagnosis, and EVD subtype (WHO, 2015).

**Pathogenesis and transmission**

The transmission of Ebola virus is due to close reside with the wild animals like chimpanzees, baboons, African green monkeys, duikers and fruit bats (Myonyctes torquata and Pteropusidae, Hypsignathus monstrosus, Epomops franqueti).[11] The possibility of sexual transmission owing to the presence of EBOV RNA in semen and vaginal secretions[12] Plants, birds and arthropods were become as possible reservoirs of ebola virus. EVD outbreaks (2001 and 2003) with traces of ZEBOV were found in the carcasses of chimpanzees and gorillas are the source of human infections. The first Ebola outbreak in Congo was due to re-usage of unsterilized needles and syringes were a crucial factor in the transmission of Ebola virus. The Kikwit outbreak of Ebola virus was because of improper protective measures of several clinicians.[13] The fatality of EHF was due to the evidence of the increase of interferon-alpha and gamma, interleukin 2 and 10 and tumor necrosis factor in blood. More noticeable effects caused by Ebola virus include changes in vascular permeability, micro vascular damage and activation of the clotting cascade and also involve in impairment of endothelial cells and platelets cause imbalance of homeostasis. The persistence of virus in semen up to 7 weeks it indicates that the probability of ebola transmission in sexual mode. The spread of EBOV infection to infants through breast milk, making the kid infected.[14] Transmission does not occur during the incubation period and only occurs once an infected person present with symptoms. In Burial ceremonies mourners have direct contact with the body of the diseased person can also play a vital role in the transmission of Ebola. And there is possibility to transmit the virus through semen by men who was recovered from disease up to 3 months.[15] ZEBOV has the most severe mortality rate of 90%, where as Sudan ZEBOV (SEBOV) have shown 53-66% mortality rate[16] An incubation period of EVD is 2-21 days (Avg. 4-10 days). Severely infected patients die within 6-9 weeks after the first symptoms appear. In most outbreaks, slow disease identification leads to increasing the death rates due to unfamiliar and non-specific symptoms of new illness are difficult for physicians to identify at initial stage.

**Diagnosis**

Since the Ebola virus has been classified by the CDC as a pathogen of category A, the category that includes most dangerous pathogens causing diseases with high morbidity and mortality, viral diagnosis should be performed only in specialized laboratories with the highest level of biosafety, i.e. BSL-4. It should be fast, sensitive and specific, and the methodology used should greatly limit the possibility of exposure of a person engaged in the study to the risk of the laboratory infection. The selection of the tests is also dependent on the capabilities of performers being under different conditions, even at the site of the epidemic outbreaks. Currently, real time RT-PCR is considered as the most sensitive method, which allows for detection of the number of viral copies in specimen. Although there are other methods of virus identification. But the presence of viral RNA can be detected by polymerase chain reaction with reverse transcription (RT-PCR) even after 48 h post onset. However, it should be emphasized that due to continuous virus mutations RT-PCR method may be unreliable and results should be confirmed by other assay.
One-tube real-time RT-PCR assay was developed for identification of ZEBOV and SEBOV.\(^{(20)}\) To distinguish between Ebola virus species and strains sequencing of amplified genomic RNA can also be used.\(^{(17)}\) The enzyme-linked immunosorbent assay (ELISA) may be used to detect both antibodies as well as virus-specific antigens. Assays for the detection of antibodies are less useful because the patient often dies before the formation of specific antibodies. Therefore, they are carried out mainly for epidemiological purpose, for patients who survived this terrible disease. Positive results obtained by the ELISA can be confirmed by Western blot. Sometimes only IgM antibodies are detectable in specimen of sick person.\(^{(18)}\) Currently applied assays use monoclonal antibodies against different viral proteins, e.g. VP40. Virus isolation in cell cultures is one of the very sensitive methods. Acute phase patient sera or
postmortem tissue samples may be appropriate material for the virus isolation. Ebola virus is able to replicate in numerous cell lines and virus growth can be detected by cytopathic effect. Vero or Vero E6 cells have been used. Additionally it is also possible to use a fluorescently-labeled specific antibodies for confirmation of antigens in infected cells. Electron microscopy has also been useful in identification and detection of viral infections. The paraffin sections of autopsy material, particularly from the liver and spleen, due to the high condensation of antigens and viral particles, are useful in immune histochemical assays with the use of specific polyclonal or monoclonal antibodies. Formalin-fixed specimens are not infectious and may be sent without special precautions or refrigeration. In some cases Microarray Techniques are used to Diagnosis of EVD due to its ability to find new strains and multiplexing capacity. Next-generation sequencing (NGS) techniques is powerful tool which allow screening of pathogens and provide proper genome data. NGS methods may be useful to detect Ebola virus in situations where the clinical index of suspicion is not high or where there is low urgency for diagnostic information.

**Treatment**

First case of EVD in Guinea was reported in March 2014 by World Health Organization, according to the outbreak has continued through the year and the total number of 28,637 patients was reported as the suspected in the EVD-affected countries. Among the cases, 11,315 patients were reported death by 27 December 2015. Proper Vaccines is not developed yet while viral diagnostic methods were already developed and established in a developed countries. Vaccine and therapeutic development is play vital role to stop the EVD and protect the world from the risk which can be generated by spread of Ebola virus. There were no specific vaccine and no successful antiviral drug was available for preventing Ebola virus infection. The paraffin sections of autopsy material, particularly from the liver and spleen, due to the high condensation of antigens and viral particles, are useful in immune histochemical assays with the use of specific polyclonal or monoclonal antibodies. Formalin-fixed specimens are not infectious and may be sent without special precautions or refrigeration. In some cases Microarray Techniques are used to Diagnosis of EVD due to its ability to find new strains and multiplexing capacity. Next-generation sequencing (NGS) techniques is powerful tool which allow screening of pathogens and provide proper genome data. NGS methods may be useful to detect Ebola virus in situations where the clinical index of suspicion is not high or where there is low urgency for diagnostic information.

**Drug and Vaccine Development**

Drug development for the Ebola disease treatment started in 2002 just after 9/11 in United States, and it was supported by governmental institutes such as National Institute of Health, Some drugs are acts against EVD but still under clinical trials (Table 1) Vaccine were tested at the preclinical levels using Non–Human Primates, and the development of manufacturing process was unpredictable step for the most potentially harmful pathogens such as filovirus including Ebola virus. There is also a need to increase health workers’ understanding on Ebola disease to improve healthcare like any other viral disease.

**CONCLUSION**

Ebola virus infection has been a serious threat to human individuals due to its highly infectious and lethal behaviour since it was discovered in 1976. For Ebola hemorrhagic fever no FDA approved medicine or antiviral drugs. The spreading of disease mainly through the transmission of blood and body fluids from one person to another person and some evidence of sexual transmission are found. There is an immediate requirement perfect Molecular diagnostics of diseases. To minimize the Ebola epidemic cases is to
control the spread of the disease. Researcher investigates verity of Antiviral Drugs and Vaccines which are affordable and easily available medication for the treatment of Ebola.

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CONFLICT OF INTEREST

None.

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