

## Ebola virus disease: Emerging outbreak

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### ABSTRACT

*Ebola Virus Disease or Ebola Haemorrhagic Fever is one of the highly fatal viral disease caused by ebola virus in humans. Mortality rate as high as 90% is reported. Virus is transmitted to humans through bats and other animals infected from bats. Although Ebola Virus Disease is reported since 1976 but currently West Africa is facing the largest outbreak of disease with danger of spread to other parts of the world. More than 5000 cases with mortality of more than 2600 cases has been reported till the end of 3rd quarter of year 2014. There is no specific treatment and vaccination available till date. Mainstay for managing patient is supportive care with early fluid resuscitation and symptomatic treatment. Our main target is to prevent human transmission by educating and supporting the community.*

**Key Words:** Ebola virus disease, mortality, prevention, human, fever

### Introduction

Ebola Virus Disease or Ebola Haemorrhagic Fever is one of the highly fatal viral disease caused by ebola virus in humans. Till march 2014 ebola virus disease was limited to the restricted areas of east and central Africa. The current outbreak affecting the West Africa is largest of all the previous outbreaks. More than 5000 cases with mortality of more than 2600 cases have been reported till the end of 3rd quarter of year 2014. The disease has high case fatality rate ranging from 25 percent to 90 percent among the infected patients with average mortality being 50 percent. <sup>[1]</sup> High mortality rate is attributable to severe hypotension resulting from significant fluid loss and typically occurs in 6 to 16 days after the development of symptoms.

### Prevalance

Ebola Virus Disease was first reported in 1976 resulting in two simultaneous outbreaks, first in Nzara (Sudan) and other

in Democratic Republic of Congo. The current outbreak effecting West Africa is the largest and most complex of all previous ebola outbreaks. The most affected countries are Guinea, Liberia and Sierra leone. These countries are among the poorest economies in the world and have recently emerged from many years of civil war. These countries have severely disabled health care systems with non existant isolation wards and poorly equipped hospitals. The areas where borders of these three countries intersect are now the designated hot zone where transmission of disease is most intense and people of these countries are reinfecting each other <sup>[2]</sup> and making it difficult to control the outbreak. Now sporadic cases from other parts of world are also being reported.

### Etiology

Ebola virus disease in human is caused by the four of the five virus species that belongs to genus ebolavirus of family

filoviridae. These four species are: Zaire ebolavirus (EBOV), Sudan ebolavirus (SUVD), Tai forest ebolavirus (TAFV) and Bundibugyo ebolavirus (BDBV) Zaire ebola virus or EBOV is considered the most virulent of all the species and is associated with largest number of outbreaks.<sup>[3,4]</sup>

### **Pathogenesis and Transmission**

Ebola Virus Disease occurs by direct contact with blood and body fluids of the infected human being or other animals. Fruit Bats are the normal carrier for the virus.<sup>[5]</sup>

Human beings become infected when they come in contact with bats or other infected animals like chimpanzees, Gorilla and monkeys. Human to human transmission occurs when they come in direct contact with blood and body fluids<sup>[6]</sup> (saliva, mucus, vomitus, stool, sweat, tears, breast milk, urine and semen) of infected person. Most infected patient spread virus through blood, feces and vomit.<sup>[7]</sup>

Droplet infection can occur when the patient is very sick.<sup>[8]</sup> Although infection through intact skin is unlikely but possibility cannot be ruled out. Health care workers frequently get infected while treating the patient with suspected or confirmed disease if they don't take appropriate protective measures like masks, gown, gloves and eyes protection. Dead bodies of the infected person can also transmit the disease if proper protective measures are not taken during burial ceremonies.<sup>[2]</sup>

Patients recovered from disease can still transmit the virus through their semen for up to 7 weeks. Air borne transmission has not been reported due to low level of virus in lungs and other parts of respiratory system of primates.

After contact exposure, EBOV infect many cell types including immune cells (monocytes, macrophages) fibroblast, hepatocytes, adrenal tissue, epithelial and non epithelial cells. Virus replication occurs in very fast and efficient manner resulting in high degree of viraemia. Signs and symptoms of disease are hypothesised to be the result of infected cell death and decreased ability of immune system to respond. Available data suggest correlation between viraemia peak and level of pro-inflammatory cytokines.

### **Virology**

Ebola virus contains single stranded, non infectious RNA genomes. As all filoviruses, ebola virions are filamentous particles in the shape of a shepherd's crook of a 'U' or of a '6' and they may be coiled or branched.<sup>[9]</sup> Ebola virions are 80 nano meters in width and 14000 nm long.<sup>[10]</sup> The ebola virus structural glycoprotein (known as GP 1, 2) is responsible for the virus's ability to bind to and infect targeted cells.<sup>[11]</sup>

### **Clinical Presentation**

Disease Symptoms usually present after incubation period of 4 to 10 days but incubation period may range from 2 to 21 days.<sup>[12]</sup> Incubation period is shorter in primary (cases who travel to or work in ebola endemic areas) than secondary cases (medical caregivers, family caregivers or person involved in burial practices). Early signs and symptoms are fever, myalgia, fatigue, pharyngitis, maculopapular rash, conjunctival injection and headache. These are followed by vomiting, diarrhoea, internal or external hemorrhage, hypotension, renal failure, pulmonary edema, shock, coma and multiorgan failure.

Typical presentation of ebola virus disease is fever, maculopapular rash with anorexia and asthenia but in current outbreak gastrointestinal symptoms predominate as primary clinical presentation. Hematological tests most commonly reveals leucopenia and increased liver enzymes, as the disease progresses patients develop thrombocytopenia and prolonged prothrombin index and activated partial thromboplastin time. Fatality from ebola virus disease usually occurs within 16 days of onset of symptoms. Little is known about long term complications of ebola virus disease but available literature suggests that patients may develop prolonged alopecia, myelitis, psychosis, uveitis and recurrent hepatitis.

### **Diagnosis**

Whenever Ebola Virus Disease is suspected in a patient, travel history and exposure to wild animal should be considered. Sometimes it is difficult to differentiate Ebola Virus Disease from other diseases like Dengue Hemorrhagic Fever, Enteric Fever, Malaria, Leptospirosis, Candidiasis, Viral Hepatitis, Meningitis, Cholera, Sepsis and Rickettsial Diseases.

Laboratory findings of Ebola Virus Disease include Thrombocytopenia, Early leucopenia followed by Neutrophilia, increased liver enzymes (ALT, AST) and abnormalities in Coagulation profile such as prolonged Prothrombin time and Partial Thromboplastin Time and Fibrin Degradation Products. The diagnosis of Ebola Virus Disease is confirmed by isolating the virus from tissue culture, Reverse Transcription Polymerase Chain Reaction (RT-PCR) assay, Antigen Capture Detection Test, Serum Neutralization test and Electron

Microscopy. Detecting Antibodies against virus is most reliable test in the later stages of the disease and in the patients who have recovered from the disease.<sup>[13]</sup>

### **Treatment**

No specific treatment<sup>[14]</sup> is available for ebola virus disease. Mainstay for managing patients is supportive care in the form of fluid resuscitation and symptom specific treatment. Supportive care is reported to have survival benefits.<sup>[15]</sup> The WHO recommends aspirin and ibuprofen should be avoided for symptomatic treatment of pain as risk of hemorrhage is associated with these medications.<sup>[16]</sup> Treatment should be directed towards maintaining effective blood volume and correcting electrolyte imbalance. Patients should be properly isolated and managed in intensive care units.

Considering the magnitude and severity of current outbreak WHO, declared that it is ethical to use experimental drugs for treatment and prevention of ebola virus disease. ZMapp is a monoclonal antibody cocktail and is being used to treat Ebola Virus Disease in current outbreak.<sup>[17]</sup> Its role in treatment is still not established. The only evidence of its effectiveness is its efficacy in treating non-human primates. Favipiravir is a nucleoside analogue that has been shown to have activity against RNA viruses including Ebola virus. The results are promising in mice but human use need to be confirmed.<sup>[18, 19, 20]</sup> BCX<sub>4430</sub> is another nucleoside analogue effective to treat Ebola Virus in mouse model.<sup>[21]</sup> Gene Slicing agents like TKM-ebola and AVI<sub>6002</sub> have been proven to be effective in mouse and primate model and some safety data of AVI<sub>6002</sub> is available in humans too.<sup>[22, 23, 24]</sup>

Passive immunotherapeutic protocols especially with monoclonal antibodies are reported effective in non-primate human model and need to be evaluated.

### **Prevention and Control**

Ebola Virus Disease has high transmission rate with no specific treatment and vaccine available and has high mortality rate. So it is very important to diagnose the patients in early stage. With nearly more than 5,000 cases, there is pressing need to control this epidemic. Public health interventions including contact tracing, isolation and social education are essential steps in stopping Ebola Virus Disease ultimately saving many more lives than can be saved by individual patient care.<sup>[25]</sup> The CDC (Center for Disease Control and Prevention) is working intensively to stop the current outbreak. Every month, thousands of travelers from the affected area travel to other countries. So Clinicians need to be alert about the possibility of Ebola Virus Disease, and sick patients travelling from affected countries within last 21 days and showing symptoms consistent with Ebola Virus Disease<sup>[26]</sup> should be immediately isolated and subjected to the diagnostic tests. Persons belonging to High Risk Categories for exposure to Ebola Virus Disease such as Health Care Providers, family care givers need to be educated about the use of Personal Protective gear such as gloves, masks, gowns, visors, gum boots. Other urgent priority is to change the long standing funeral practices that require close contact with highly contagious corpses.<sup>[2]</sup> It is important that all the members of global health community - health care workers, scientists, regulators, funders, government and local communities

come together to control this emerging outbreak.<sup>[27]</sup> Timely control will require convincing community leaders and health staff that isolation and rapid burial practice are mandatory and that only trained qualified and properly equipped health care workers should have contact with deceased patients.<sup>[28]</sup>

### **Vaccine**

There are only two vaccines CAd3 – EBOV (CAd3) from Glaxo Smith Kline and US National Institute of Allergy and Infectious Disease (NIAID), and rVSVAG-EBOV-GP (rVSV) from New Link Genetics and the Public Health Agency of Canada are undergoing Phase I Clinical trial to determine the level of humoral and cellular immunity that can be induced.<sup>[29]</sup>

### **Conclusion**

The current outbreak is the largest, longest and the most fatal of all the previous outbreaks.<sup>[30]</sup> Ebola Virus Disease is becoming humanitarian and economic emergency besides the immediate health concerns. Transmissions can be interrupted by infection control measures. There is need for immediate priority for control, early diagnosis, with patient isolation, contact tracing, adherence to bio-safety guidelines in laboratories, barrier nursing procedures and use of personal protective equipment by all health care providers, disinfection of contaminated objects/area, and safe burial practices.

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