# Ebola virus explained essay

Introduction

Ebola virus is one of the most virulent and lethal pathogens known to human. Ebola virus epidemics have emerged from time to time since it was first discovered in 1976 from the Democratic Republic of Congo, formerly known as Zaire, but the largest known Ebola virus outbreak up to date is ongoing at the time of writing this article, in West Africa. Approximately 550 000 cases are estimated to be reported from Sierra Leone and Liberia by the 20 $^{th}$ of January 2015. The transmission of the infection to a number of countries including Guinea, Liberia, Sierra Leone, Nigeria and occasional cases being reported from USA, Canada, Netherland and India reveal the potential of the infection to get spread worldwide. Despite this disease being highly contagious, life-threatening, and no specific treatment being found, it can be prevented with the use of proper infection prevention and control measures. The study of the Ebola virus disease is important as that knowledge will pave the way for the reduction of victims, the invention of an effective drug and will also be useful in the management of a similar epidemic.

Virology

Ebola virus is a member of the family Filoviridae. As the name implies the virus is filamentous in shape. Marburg virus and Ebolavirus are the two main genera of the viral family which are medically important. Viruses of these two genera are studied and presented together due to their many similarities in the life cycle, the primary reservoirs, ways of transmission, clinical presentation, treatment and prevention measures. The only noted difference

is that the Marburgvirus is spread by bat species adapted to open forests such as savannah whereas Ebolavirus is spread by bat species adapted to deep rain forests(1).

Five subtypes of Ebolavirus namely, *Ebolavirus zaire, Ebolavirus sudan, Ebolavirus reston, Ebolavirus cote d' Ivore,* and *Ebolavirus bundibugyo* have been identified and named after the area in which they were first discovered(1). Of these *E. Zaire* was the first to be isolated and studied(1) and it is responsible for the most number of outbreaks(1) including the latest outbreak in 2014 before which *E. sudan* accounted for ¼ of all Ebolavirus deaths(1). Except for the slight lower fatality rate, *E. sudan* is more or less similar to *E. zaire.* The case fatality rate of E. sudan is reported as 40-60% and that of E. zaire as 60-90% (3).

Transmission

Ebola is initially transmitted to human as a zoonosis. Various species of fruit bats found throughout central and sub Saharan Africa as hosts (2),( 4). Contact with bats through bites and scratches or exposure to their secretions and excretions through broken skin or mucous membranes can cause the infection in humans (2), (4). The infection can also be transmitted through other end hosts. Those recorded from Africa are forest antelopes, porcupines, chimpanzees, gorillas, monkeys and other non-human primates. Attacks during hunting these animals or handling infected animal carcasses have resulted in the introduction of the virus to the human population from the wild (1). The outbreak of the epidemic begins with the subsequent transmission of the infection from the index case to secondary individuals.

An outbreak often begins from a single introduction to a human from the wild, which involves virus variants of little genetic diversity. Records reveal that outbreaks stemmed from multiple introductions lead to distinct chains of human to human transmission with a greater diversity in the virus variants(5).

EVD is highly contagious. The infection may spread in the community and in the hospital environment through direct contact with infected body fluids such as blood, secretions and excretions or tissue of an acute patient or through direct contact with contaminated materials like clothes and bed linen(1). One major reason for the rapid spread of the epidemic is the traditional funeral rituals, which include cleansing of the cadaver, removal of hair finger nails, toe nails and clothing. People taking care of infected people including health care staff also have a high risk of contracting the disease. Moreover semen of male survivors is said to remain infectious for up to 82 days after the onset of the symptoms. As long as the virus remains in the body fluids the person remains infectious. Airborne transmission of Ebola virus is strongly suspected but is not yet experimentally proven.

Clinical Presentation

EVD caused by different strains of Ebola virus bring about different clinical features. Incubation period of Ebola virus is generally considered as 2 – 21 days. (1, 3) Ebola virus disease shows various acutely developing constitutional prodromal symptoms which lead to a wide range of differential diagnosis including not only other viral haemorrhagic fevers, but also malaria

(3), typhoid (3), cholera (1), other bacterial rickettsial and even non-infectious causes of haemorrhage.

The evolution of the disease resembles that of a severe haemorrhagic fever. Patients present with high fever, temperatures being as high as 39-40 $^{0}$ C (3, 6), body aches and fatigue (3). Subsequently gastrointestinal symptoms such as epigastric pain nausea, vomits and /or diarrhoea without blood appear if fever persists until day 3 – 5 (6).

After 4 – 5 days of illness (4) a macular rash may appear but it may not be clearly noticeable on dark skin (1). After this stage haemorrhage from different sites begin. Bleeding from both upper and lower digestive tract, respiratory tract, urinary tract, vagina in females can be observed (1, 3). Further petechiae on the buccal mucosa, skin and conjunctivae develop. Recurrent episodes of vomiting which prevents any oral intake of fluids and large amounts of watery diarrhoea (5 or more liters per day) (6) contributes to a massive fluid loss leading to dehydration. If fluid replacement is inadequate, prostration, severe lethargy and ultimately hypovolaemic shock follows.

Hypovolaemic shock has been reported in 60% of the cases (6). Despite the high body temperatures, patients acquire cold extremities due to peripheral vasoconstriction. Rapid and thready pulses, tachypnea, oliguria or anuria can be observed (6). Simultaneously features such as asthenia chest and abdominal pains, pains in muscles and joints and headaches develop. Although in some cases cough and dyspnea occur due to pulmonary haemorrhages, other respiratory symptoms except for hiccups are

uncommon (6). Conjunctival injection is a common clinical feature. Neurologic symptoms that are usually seen are hypoactive and hyperactive delirium characterized by slowed cognitive functions, confusion, agitation and rarely seizures (6). As the disease evolves internal bleeding can also start but generally by this time patients are already in a state of coma (1).

It is reported that only 5% of the patients present with haemorrhage from gastro intestinal tract before death. Most of the reported deaths have occurred due to shock during the 7 $^{th}$ to 12 $^{th}$ day of illness. Symptoms of 40% of the patients have improved around the 10 $^{th}$ day though symptoms like oral ulcers and thrush have developed. Most of the patients who survived up to the 13 $^{th}$ day have shown a higher chance of ultimately getting recovered. Some patients who showed initial improvement of symptoms have developed neck rigidity and lowered levels of consciousness which are associated with late mortality.

Pathology

Examination of autopsies and post-mortem biopsies is extremely useful in the study of the pathology of the ebola virus disease. Due to the biosafety risk to the autopsy personnel when handling specimens, pathological descriptions of only a limited number of cases are available (7).

A common finding of Haematoxilin and eosine stained tissue sections is oval shaped or filamentous eosinophilic intracellular inclusions which are formed by the aggregation of nucleocapsids of the virus. These inclusions can be detected in macrophages, hepatocytes, endothelial cells, connective tissue

fibroblasts etc. Immunohistochemical stains reveal viral antigens in cells of various infected tissues including macrophages, dendritic cells, epithelial cells of sweat and sebaceous glands, interstitial and tubular cells of the kidney, seminiferous tubules, endothelial cells and endocardial cells. In addition necrotic cells and cell debris contain antigens in large quantities. Electron microscopy exhibits abundant free virus particles in alveolar spaces, liver sinusoids, and interstitial cells of the testis and in dermal collagen. Karyorrhexis and apoptosis are seen in the cells of the portal triads, macrophages of the red pulp of the spleen and in the tubular epithelial cells of the kidney (7).

Liver tissue shows the most symptomatic histopathological features including focal or widespread necrosis of hepatocytes and mild steatosis. Although usually inflammation is minimal, hyperplasia of kupfer cells and infiltration of mononuclear inflammatory cells is seen. Infected lung shows congestion, haemorrhage and intra-alveolar oedema but inflammation is not significant. Mild focal infiltrates of mononuclear inflammatory cells are known to occur in the lamina propria of the stomach small intestine and the colon. Skin biopsies reveal dermal oedema, focal haemorrhages, petechiae, ecchymoses, and macular rashes. The spleen and lymph nodes exhibit widespread lymphoid depletion due to apoptosis and necrosis. Inflammation of the kidney is not evident although acute tubular necrosis is a usual finding. Even though the endocardium of the heart contains viral antigens, the myocardium does not show any significant damage. Brain histology shows panencephalitis and perivascular infiltration of lymphocytes (7).

Prevention

World Health organization (WHO) has recommended a set of infection prevention and control measures for health-care workers that include precautions that should be taken at different stages of managing EVD patients

Standard precautions

Regardless of the diagnosis it is recommended for health-care workers to take standard precautions when handling all patients, as it is difficult to identify EVD patients during early stages of the disease. These are,

- Performing hand hygiene
- Using disposable gloves before touching materials probable of being contaminated with virus
- Wearing eye protection and gown before involving in procedures which have a possibility of body fluids being projected.

Hand hygiene

Hand hygiene must be performed using soap and water or alcohol-based hand rub solution, following WHO recommended technique,

- before wearing gloves and personal protective equipment (PPE)
- after an exposure to a patient’s body fluids
- after a contact with a contaminated surface or equipment
- after removing PPE.
- if hands are visibly soiled

Personal Protective Equipment (PPE)

PPE should be worn before entering EVD patients’ care areas according to the recommended order by WHO and removed before leaving the care area. Contact of a used PPE with any part of the face or non-intact skin should be avoided. The PPE includes,

- Non-sterile gloves of the correct size
- Impermeable and disposable gown with long sleeves
- Face shield
- Puncture resistant and impermeable closed shoes

Patient placement and management

Suspected or confirmed EVD patients should be isolated and if possible kept in single rooms. If not they must be placed in beds with at least 1m gap in between. Visitors must be restricted except for those who are needed for the well-being of the patient such as a child’s parent.

Management of used equipment and other materials

It is recommended that equipment like stethoscopes should be decontaminated and sterilized before reuse, if separate equipment is not available. Parenteral medication equipment, surgical blades, syringes and needles should never be reused. They should be disposed in puncture resistant bins. All non-sharp solid waste should be disposed in to leak-proof bags or bins.

Used linen should be collected in leak-proof bags kept at the place of use. They should be washed with water and detergent, rinsed, soaked in 0. 05% chlorine for 30 minutes and then dried.

All bins must always remain upright and should be sealed when ¾ full. Before being taken out of the wards the outer surfaces of these containers must be disinfected using 0. 5% chlorine.

Environmental cleaning

Cleaners should wear heavy-duty rubber gloves, and impermeable, puncture proof boots in addition to the PPE. Water and detergent must be used to clean the work surfaces and floors of the hospital. This should be practiced at least once a day. Other contaminated surfaces and objects must be cleaned and disinfected using 0. 5% chlorine.

Handling of biological material

Performing autopsies, *post-mortem* biopsies and other laboratory tests of tissue samples of EVD confirmed or suspected patients should be minimized and should only be performed by trained personnel. Full PPE must be worn during handling specimens. All specimens should be delivered in clearly labeled, leak-proof, non-breakable, containers with disinfected outer surfaces.

Dead bodies must never be washed or embalmed. They should be sealed in double bags, disinfected with 0. 5% chlorine and buried promptly. Some cultural and religious rituals can be adapted if needed, but handling of the body must be kept to a minimum and full PPE must be worn at all times.

In case of exposure to infected body fluids

All current tasks must be safely and immediately stopped and PPE must be removed safely. Affected skin should be washed with soap and water and any affected mucous membranes like conjunctiva should be washed off with a plenty of running water. The person should be checked for fever and other symptoms for 21 days.

Pathogenesis

Pathogenesis of Ebola virus shows a similarity to that of most of the other filoviruses which involves immunosuppression, increased vascular permeability and coagulopathy (7, 18). Ebola virus enters the host though abrasions of the skin, though mucous membranes or though injection by accident. The virus enters monocytes, macrophages and dendritic cells and gets carried away via lymphatics to the circulation. It then spreads to the liver and spleen infecting tissue macrophages and fibroblastic reticular cells. The main cellular targets of the virus are macrophages, dendritic cells and kupfer cells. Ebola virus shows interaction between varieties of cellular proteins which is why the infection is characterized by broad tissue and organ tropism.

Immunopathology

In most of the viral infections immune system plays a major role in containing the infection from spreading. However the tissues and organs of fatal EVD cases show minimal inflammation, suggesting of impairment in the immune responses.

It has been found that structural proteins of filoviruses *e. g.* VP24 (Virion protein) and VP35 inhibit interferon responses and thus evade the host innate immunity. As previously mentioned, apoptosis of natural killer cells and T lymphocytes is revealed in histopathology which explains the suppression of the adaptive immune responses.

As in many severe infections, Ebola virus infection also causes a massive release of pro-inflammatory mediators and vasoactive substances. Even though the pro-inflammatory mediators promote inflammation and coagulation, the systemic spread of the infection is not effectively controlled. This is probably due to the vasodilation mediated by the vasoactive substances.

Endothelial dysfunction and coagulopathy

The virus invades endothelial cells and endocardial cells and causes injury (18). This results in internal haemorrhage, fluid and electrolyte imbalance and cardiovascular failure. Endothelial damage results in the platelet aggregation and consumption. The increased level of pro-inflammatory factors and the increased production of surface tissue factor protein in infected monocytes and macrophages promote the coagulation cascade. Due to the hepatocellular damage the production of coagulation factors, fibrinogen, protein C and S are also decreased . Collectively this results in disseminated intravascular coagulation.

Other socio-economic problems related to Ebola virus epidemics

When considering the current outbreak, in addition to the huge number of lives that has been succumbed to the disease, it has created many other critical problems not only in Ebola hit countries, but in other African countries as well.

Agriculture has the biggest contribution to the African economy. As many farmers have died of the epidemic and many have abandoned their farmlands in the fear of catching the disease, there is a huge labour shortage in these countries and a fall of food production. An emergence of a food scarcity in the near future is predicted by experts.

Chocolate producing companies and many other industries are greatly affected by labour shortage. Nigeria and Ivory Coast are major cacao producing countries but most of the workers are migrants from Liberia and Guinea. International companies like Nestle and Mars have launched education and fundraising programmes to prevent the spread of the infection among cacao workers.

Many schools have been closed owing to the deadly infection surging through the country. Besides the impact on education, the feeding programme carried on by the governments for children has come to a standstill as a consequence.

Tourism is another sector hit by the epidemic. Even though Africa is a large continent bigger than Europe, USA and China combined; tourists tend to see it as a single country since the Ebola epidemic has emerged. For instance, Tanzania, a famous wild life destination is an East African country, more than

6000 miles away from an Ebola hit land. It is reported that hotels of Tanzania have lost 50% of bookings for 2015 (21).

Many African countries refuse to host international events and conferences due to the risk of the Ebola epidemic being introduced. For example, Morocco, the host of African Cup of Nations, which is scheduled to January 2015, requests a postponement. The government says, “ There is no way we can be lenient with the health and safety of the Moroccan citizens” (24).