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Ebola Virus and its Public Health Significance: A Review

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Review Article

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Abstract

Ebola virus disease is a severe, often-fatal, zoonotic viral disease in humans and Nonhuman primates (NHP) like monkeys, gorillas and chimpanzees. Ebola is RNA virus that belongs to the family filoviridae, genus Ebola virus. The viruses (EBOV) are enveloped, non-segmented, negative-sense, single-stranded RNA viruses. Ebola virus disease (EVD) was first described in the Democratic Republic of Congo (DRC) in 1976. 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 includes; fever and headache, followed by vomiting and diarrhea. Patients in the final stage of disease die in the clinical picture of massive bleeding, severe dehydration, 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 Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). No specific treatment has been demonstrated yet to be safe and effective for Ebola virus. Standard treatment currently consists of supportive therapy, including maintenance of blood volume and electrolyte balance, as well as standard nursing care. Prevention and control is mainly based on appropriate precautions to break ways of transmission. Despite the fact that no detection of the virus had been discovered in Ethiopia so far, it is in medium risk country because of most people travelling from West Africa to South Africa travels via these countries. But, there is lack of updated information on Ebola virus and its zoonotic importance. All the necessary precautions should be made to prevent the virus from entering the country and thus 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.

Keywords: Ebola virus; Hunting; Monkey; Prevention; Zoonotic

Introduction

Ebola virus (EBOV) is RNA virus that belongs to the family Filoviridae, genus Ebola virus. The viruses (EBOV) are enveloped, non-segmented, negative-sense, single-stranded RNA viruses. The virus is recognized as a significant warning to public health, since they cause periodic human and non-human primate outbreaks with high mortality rates. Ebola virus disease is a severe disease that causes hemorrhagic fever in humans and animals. The diseases are often fatal as they affect the body's vascular system. This can lead to significant internal bleeding and organ failure [1].

The virus was first discovered in 1976 near the Ebola River in Zaire what is now the Democratic Republic of the Congo (DRC). Since then, outbreaks of Ebola along with human's have appeared sporadically in Africa and Currently Ebola viruses are found in several African countries. Up to now five species of Ebola virus have been identified: *Zaire Ebola virus* (ZEBOV), *Bundibugyo Ebola virus* (BEBOV) (found in Uganda), *Tai Forest Ebola virus* (TFEBOV)(formerly known as Cote d'Ivore), *Sudan Ebola virus* (SEBOV), and *Reston Ebola virus* (REBOV) (found in Western Pacific, highly pathogenic in nonhuman primates)[2].

All species originating from Africa cause Ebola Virus Disease (EVD) in humans and non human primates (NHPs).The only species not originating from Africa, the *Reston Ebola virus* was isolated for the first time in monkeys (*Macaca fascicularis*) imported from the Philippines to a quarantine unit in Reston, United States, in 1989p [2]. Ethiopia has no reported Ebola outbreaks as yet, but it is in medium risk country along with Nigeria and Kenya because of most people travelling from West Africa to South Africa travels via these countries [3].

Despite numerous attempts to locate the natural hosts, the reservoir of Ebola viruses was undetermined until rec ently when Ebola virus was detected in bats in Africa. In 2 005, the first direct evidence from different studies that bats were reservoir hosts for Ebola virus was reporte d [4].

In Africa, fruit bats such as *Hypsignathus monstrosus*, *Epomops franqueti*, and *Myonycteris torquata* were found as the natural hosts of the EBOV. Non-human primates, such as apes, monkey and gorillas can be infected by feeding on the partially eaten fruits and acquire the infection, which can be then be transmitted to humans [5].

Transmission of EBOV occurs through close contact with skin and secretions of an individual suffering from active infection. Urine, saliva, sweat, feces, vomitus, breast milk, semen, and virus-contaminated objects can transmit the infection as well. There is no evidence for aerosol transmission although it cannot be excluded [6]. The incubation period of EBOV is five to nine days with a range of 1-21 days. EVD is quickly progressive disease with multisystem involvement, causing bleeding and coagulopathy. The most frequent clinical findings are fever, nausea, vomiting, diarrhea and fatigue. The causes of death are multi-factorial and include massive hemorrhage (bleeding occurs in up to 50 %), hypovolemia and electrolyte imbalance, severe sepsis and multi -organ failure [7].

No specific antiviral treatment has been demonstrated yet to be safe and effective for Ebola virus disease. Standard treatment currently consists of supportive therapy; including maintenance of blood volume and electrolyte balance, as well as standard nursing care [8]. Because the full host range of Ebola may not be known, all sick and dead wild animals should be avoided (including for use as food) [9].

Even though no detection of virus had been discovered in Ethiopia, it is categorized under medium risk country and there are hosts capable of transmitting EVD. But, there is scarcity of updated of information on Ebola virus and its zoonotic importance. Thus, the objective of this paper is; to review the Ebola virus, Zoonotic importance and its impacts.

Review on Ebola Virus and its Public Health Significance

Historical Background of Ebola Virus

Many emerging and reemerging human pathogens are derived from animals or from animal tissues, waste, or products. EBOV are among the most deadly emerging zoonotic diseases. The zoonotic potential of these viruses was identified at the time of their discovery during the first recognized filovirus in 1976 near the Ebola River in the Democratic Republic of the Congo (DRC) [10]. Ebola are recognized as a significant threat to public health and conservation as they cause periodic human and non-human primate outbreaks with high mortality rates. Since 1967 when Marburg virus first emerged in humans, their importance as lethal pathogens causing hemorrhagic fever has been appreciated, but their origins, natural history, and ecology remained elusive for decades. In

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2005, the first direct evidence from field studies that bats were reservoir hosts for *Ebola virus* was reported [11].

Etiology

The family *Filoviridae* consists of three genera, *Ebola*, *Marburg* and *Cueva virus.* Ebola and Marburg viruses are among the most virulent pathogens in humans [5]. In the past, Ebola and Marburg viruses were classified as hemorrhagic fever viruses, based upon their clinical manifestations, which include coagulation defects, bleeding, and shock. However, the term hemorrhagic fever is no longer used to refer to Ebola virus disease since only a small percentage of Ebola patients actually develop significant hemorrhage, and it usually occurs in terminal phase of fatal illness, when the individual is already in shock [12].

Genus Ebola is divided into five identified species, four of which have caused disease in humans. They are Ebola virus (*Zaire Ebola virus*); Sudan virus (*Sudan Ebola virus*); Taï Forest
virus (*Taï Forest Ebola virus*, formerly *Côte d'Ivoire Ebola v irus*); and the Bundibugyo virus (*Bundibugyo Ebola virus*). The fifth, Reston virus (*Reston Ebola virus*), has caused disease in nonhuman primates but not in humans [13].

Morphology

Viruses in the family Filoviridae are mononega viruses, which mean they have an unsegmented genome with negative polarity. Based on the differences in the genetic make-up, there are two genera in this family: Marburg virus and Ebola virus. Marburg virus has no soluble glycoprotein (sGP) which Ebola do have and may be connected with the regulation of its pathogenicity [14].

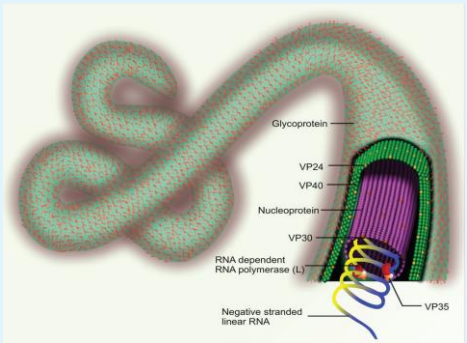

Figure1: Structure of Ebola virus and its genome [5].

There are seven expressed proteins by filoviruses: nucleoprotein (NP), glycoprotein (GP), RNA-dependent RNA polymerase (RdRP), and four structural proteins: viral protein 24 (VP24), viral protein 30 (VP30), viral protein 35 (VP35), and viral protein 40 (VP40). The ribonucleoprotein is derived from the RNA genome, NP, VP30, VP35, and RdRP protein, though Marburg virus is reported to be able replicate in the absence of VP30 [15]. The VP35 protein is known to block interferon induction in both Marburg and Ebola viruses [16].

Life Cycle

The natural reservoir host of Ebola virus remains unknown. However, researchers believe that the virus is animal-borne and bats are most likely reservoir. Molecular studies have demonstrated that bats are natural reservoir host for several recently emerged Ebola viruses [17]. However the role of primates in the natural ecology of Ebola virus is still poorly understood and their role as part of a reservoir complex is unknown. Human disease is frequently linked to contact with infected primate carcasses, though direct contact with other infected hosts is reported [18]. It is not clear whether ther e is primate to primate transmission. However, it is noticeable that primates, especially great apes, appear to have been severely affected by Ebola (*Zaire Ebolavirus*) [19].

Epidemiology

Ebola virus typically appears in sporadic outbreaks, usually spread within a health-care setting. There is increasing frequency of outbreaks in sub-Saharan Africa of which significant ongoing outbreaks in wild (endangered) non-human primate species (chimpanzees) [20]. The important Ebola sources for humans are animal carcasses in the forest [21]. The increasing contact of the human and virus reservoir, combined with its virulence has enhanced EVD epidemics [22]. The virus is zoonotic (animal borne) with four of the five subtypes occurring in an animal host native to Africa except Ebola-Reston subtype, which was isolated from infected *cynomolgus* monkeys that were imported to the United States and Italy from the Philippines [23].

Risk factors

Host related risk factors: The most important risk factor was direct repeated contact with a sick person's body fluids, as it occurs during the provision of care. There is a specific risk for healthcare workers, especially if involved in caring for Ebola hemorrhagic fever patients (e.g. volunteers). However, the level of precaution taken in such settings should effectively prevent the transmission of the disease. There is also high risk

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through unprotected sexual contact with a patient that has recently recovered from the disease [24] Individuals considered at risk for Ebola virus includes persons with a travel history to sub-Saharan Africa, persons who have recently cared for infected patients and animal workers who have worked with primates infected with African-derived Ebola subtypes [25].

Ebola virus infection has no sexual predilection, but men and women differ with respect to the manner in which direct exposure occurs. Men, by the nature of their work exposure in forest and savanna regions, may be at increased risk of acquiring a primary infection from gathering "bush meat" for food. Because women provide much of the direct care for ill family members and they process the bush-meat for conservation and meal preparation, they may be at increased risk of acquiring Ebola virus infection. They also mourn the dead with tendency to physical contact with corpse. However, men and women who are medical healthcare providers seem to share a high and equal risk of infection [26].

Vector Related Risk Factors: The greatest mysteries regarding the Ebola viruses are the identity of their natural reservoir(s) and the mode of transmission to wild apes and humans [27]. Ebola virus sequences, not infectious virus, have been detected in samples collected from bats in Central Africa [28]. However, studies suggest that bats are the reservoir hosts of Ebola viruses in Africa [21]. Bats live on average 3.5-times longer than a mammal of similar size. This promotes the persistence of the virus in the host and increasing likelihood of transmission makes them particularly suitable reservoirs for viruses [29].

The Virus has ability to infect domestic animals without causing disease, which could in the future become reservoirs and cause a new type of zoonotic transmission in humans [30].

Figure 2: Fruit bat, reservoir host of Ebola [31].

Environmental risk factors: The known geographic range of primary Ebola virus infection is in tropical Africa with the exception of Reston Ebola virus, which occurs in Philippines [32]. The climate change can affect wildlife habitats and increase the frequency of disease outbreaks [33]. The onset of EVD usually occurs in dry season. It has been suggested that dry season has been extended due to deforestation of the area over decades and environmental reports have suggested an extremely dry season in Guinea during the period of the epidemics [19]. Before Ebola hit, hunger was already a problem in the affected countries, particularly in rural areas. Without sufficient access to food, hunger often compels people to continue hunting and eating animals despite the risks [34].

Out breaks

No.	Year of Outbreak	Countries	Species	References
1	The 1976-1979	Sudan and DRC	*E. Sudan* and *E. Zaire*	[35]
2	1994-1997	Zaire and Ivory coast	*E. Zaire, E. Sudan and E. Ivory coast*	[36]
3	2000-2004	Sudan and Uganda, Gabon and DRC	*E. Sudan, E. Zaire, E.Bundibugyo*	[37]
4	2014	Guinea, Sierra Leone, Liberia and Nigeria	*E. Zaire, E. Sudan, E. Ivory coast*	[38]

Table 1: Ebola virus out breaks with their respective countries and species of Ebola.

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Transmission

There are two main modes of transmission of Ebola virus into human populations. Either direct contact to a reservoir or contact to other wildlife that also contracts EBOV from the reservoir [39]. Demonstrating direct transmission from putative reservoirs, such as bats, is difficult because of the nature of bat bites, which are often invisible and painless, but evidence for this route, even though circumstantial, is po werful [40]. The Transmission of EBOV to humans in sub-Saharan Africa thought the contact with dead or living infected animals (non-human primates, antelopes and bats). Once Ebola virus has infected humans, they can spread from person to person [19].

Transmission principally happens by direct contact with infected blood, as it can contain large amounts of virus that contaminate the environment if patients hemorrhage or other bodily fluids (saliva, sweat, semen, milk, tear, feces), and tissues from dead or living infected persons [41]. The virus is often spread through families and friends because they come in close contact with such fluids when caring for infected persons [37]. Transmission through inanimate objects (bedding, clothing) contaminated with infected bodily fluids is also possible [42].

Animal Food Products and Ebola Virus Transmission

Bush meat: The exact nature of animal-to-human transmission of Ebola viruses is not often known. However, harvesting food product is directly related to Ebolavirus transmission. Specifically, hunting and butchering of wildlife for food typically referred to as "bush meat," exposes humans to blood and other fluids of potentially infected animals. Studies have found that bush meat is an important source of cash income and a food source in West Africa, particularly during times of economic hard ship [43]. The international market of illegal bush meat poses public health risks as USA and European countries demand for bush meat [44].

Livestock: It is hypothesized that livestock could be a possible Ebola virus reservoir, but no cases have been reported. The Food and Agriculture Organization (FAO) has characterized current knowledge by stating, "Information is extremely limited on the ability of the Ebola virus to infect livestock like cattle, sheep and goats or chickens [45]. Guinea pigs, consumed in several countries, are commonly infected in Ebola virus research. Recent studies have also shown that swine can become infected with the highly pathogenic EBOV. Once the pigs became infected they developed clinical symptoms and transmitted the virus to healthy pigs [46]. There is strong evidence that dogs, which are consumed in some countries including some with EVD outbreaks, can become infected with EBOV naturally [47].

Plant Food Products and Ebola Virus Transmission

Consumption of Contaminated Plant Food Products: T here are no known cases of EVD transmission via consumption of plant food products. However, there may be transmission in the same way that an Ebola virus may be transmitted to nonhuman primates through fruit partially eaten by bats [48]. Some experts speculate that Ebola virus could be transmitted via bat saliva or feces on fruit such as mangoes or guava. The concern is great enough that in the Ebola affected nations, United Nation International Children's Emergency Fund (UNICEF) advises not to eat mangoes that "have been bitten by bats" [49].

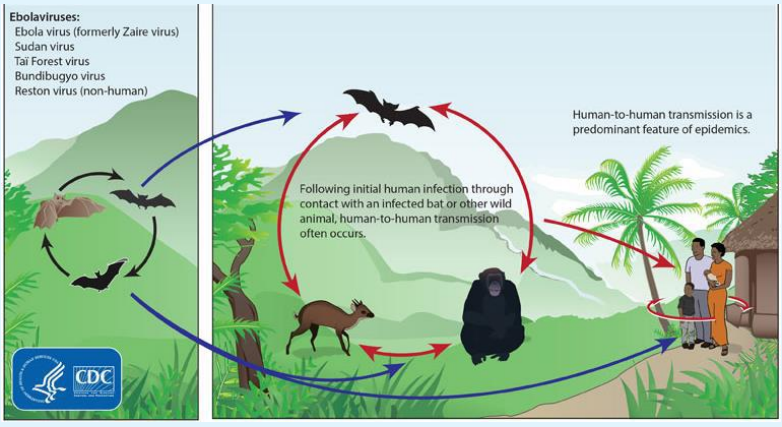

Figure 3: Zoonotic and Transmission of Ebola virus [50].

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Pathogenesis

The pathogenesis of Ebola is still not well understood because of the difficulty in conducting clinical studies under the conditions of outbreaks [51]. The Ebola virus enters the host through small skin lesions or mucosa. Upon cell entry, the virus replicates in the host cell membranes and the infected cell is destroyed [52]. Analysis of tissues from infected human and non-human primates have demonstrated that viral replication occurs initially in leukocytes, epithelial cells, hepatocytes, spleen, adrenal cortical, and endothelial cells [5].

The pathogenesis of Ebola virus can is divided in to two mechanisms, those in which viral infection of host cells results in direct damage to tissues, and those in which tissue injury is brought about indirectly, through interactions between the virus and the host immune systems. The two factors are important for the virus to be able to kill a variety of cells in many different tissues [53]. Antigen presenting cells (APCs) such as macrophages, monocytes and dendritic cells are the first cells to be infected by the virus [5].

Viral protein 35(VP35) and Viral protein 24(VP24) cause functional dysregulation of the APCs, preventing them from presenting antigens to naïve T cells and blocks the maturation of dendritic cells. The loss of function of the APCs causes massive apoptosis of lymphocytes [54]. The systemic inflammatory response causes fever and the recruitment of more APCs to the site of infection; this results in the spread of infected cells to secondary lymphoid organs, lungs, liver, and other sites of viral replication [55]. Hepatocellular necrosis impairs liver functions and reduces the synthesis of coagulation factors and severe coagulation changes are observed in Ebola infections [56].

If the adrenal glands are affected, this causes sodium depletion, secondary hypotension and hypovolemia. Infected epithelial cells lining the gut cause gastrointestinal symptoms during the early stages of infection (e.g. vomiting and diarrhea) [5]. Despite direct damage to organs, the severity of the disease is due to a large extent to the uncontrolled inflammatory response that causes an increase in vascular permeability, vasodilation and a loss of endothelial function which results in multi organ dysfunction [13].

Clinical Sign

The incubation period of the Ebola virus ranges from 2 to 21 days [57], differing between the different species of the virus and also depending on the type of transmission (6 days for percutaneous transmission, 10 days for contact transmission [58]. Initially, patients manifest symptoms such as fever, fatigue, headache and myalgia. Later, multi-system impairment can be verified, with involvement of the gastrointestinal (nausea, vomiting, diarrhea), cutaneous (maculopapular rash), respiratory sy stems (coughing, dyspnoea), neurological and vascular systems resulting in shock [57].

Hemorrhagic manifestations (petechiae, bleeding in the mucous membranes and venipuncture sites, hemoptysis, nose bleeding, hematemesis) can be observed at the peak of disease. The most commonly described symptoms are fever in combination with anorexia, diarrhea, vomiting, abdominal pain, asthenia and maculopapular rash between day 5 and 7 after the onset of the disease [59].

Diagnosis

The most important method for diagnosis of EVD is via the medical history of the patient, especially travel and occupational history and exposure to wild animals such as fruit bats. One challenge in the diagnosis of Ebola is the fact that it mimics other diseases such as malaria and typhoid fever, given its initial non-specific symptomatology [60]. According to the Center of Disease Control (CDC), a possible case of Ebola virus must be considered if the following two criteria are present: 1**-**presence of fever or subjective sensation of symptoms such as headache, asthenia, vomiting, diarrhea, abdominal pain and bleeding; and 2**-** presenting an epidemiological risk during the 21 days preceding the onset of symptoms. Epidemiological risk is understood, for example, as having traveled to a country undergoing rapid dissemination of the virus, having contact with a symptomatic Ebola patient or with animals infected with the virus. The virus only reaches detectable levels in the blood 3 days after the onset of symptoms [13].

Laboratory diagnosis of Ebola virus infections can basi cally achieved in two ways. Measurement of host-specific immune responses to infection, and detection of virus particles (RNA and protein) in infected individuals. Reverse transcriptase polymerase chain reaction (RT-P CR) and antigen detection Enzyme- linked Immuno sorbent assay (ELISA) are the primary test systems to detect the virus particles (RNA and protein) in the blood and body fluids. For antibody detection, the most commonly used assays are direct immunoglobulin G (IgG) and immunoglobulin M (IgM) response to infection by ELISA [37].

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In primates, the virus occurs 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. In bats, Ebola viruses have been found in tissues such as the liver and spleen and sometimes in the blood [37].

Treatment

There is still no licensed safe and effective treatment for Ebola virus disease. Current treatment is merely supportive, involving measures to control, pain and secondary infections, as well as fluid therapy [61]. Symptoms of EVD and its complications should be treated as they appear. Hypovolemia due to massive fluid loss via vomiting and diarrhea is the most common symptom of EVD and Clinical management should focus on maintaining fluid volume and correction of electrolyte abnormalities and it's necessary to monitor daily fluid input and outputs. It was also observed that antiemetic and antidiarrheal drugs may limit massive loss of fluids from gastrointestinal tract and they should be considered [62].

If disseminated intravascular coagulation develops, replacement of coagulation factors, correction of thrombocytopenia and anemia is necessary. On the other hand respiratory failure is more often secondary to EVD complications and therefore, oxygen therapy in severe cases should be used [63].

Control and Prevention

Given that there is no specific treatment for Ebola, prevention is a crucial aspect to avoid the virus from spreading. 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). International health regulations require that, nations report acute hemorrhagic fever syndromes immediately to World Health Organizations (WHO) witho ut waiting for the causative agent to be identified to prevent transmission and aid in case management and diagnosis [9].

Preventive measures should be directed above all toward avoiding inter-human transmission. It is necessary to isolate the patient and take immediate steps to institute strict containment nursing practices. Avoiding contact with material or bodily fluids from people infected with Ebola are some of the measures. Health professionals should wear personal protective equipment and apply appropriate control measures. There are also monitoring and tracking protocols for travelers from West African countries affected by Ebola [13].

Consumption of wild animals is common practice, particularly in areas with high food insecurity. Health officials have to inform the public about the risks associated with eating wild animals, including fruit bats and other animals that might carry Ebola virus disease [34]. Avoid contact with bats and nonhuman primates or blood, fluids, and raw meat prepared from these animals [13]. 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. So, Sexual abstinence has been recommended for at least t hree months after recovery [64].

Status of Ebola Virus in Ethiopia

Ethiopia has no reported Ebola outbreaks as yet, but it is in medium risk country along with Nigeria and Kenya because of most people travelling from West Africa to South Africa travels via these countries [3]. 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 [24].

The Federal Minister of Health (FMoH) organized the orientation workshop taking attention 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 [64].

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 countr ies. The airline also requires the passengers to fill in surve illance forms before boarding for traceability purposes; a nd precautionary testing is being conducted by health officials on passengers before boarding and after arriving [3].

Conclusion and Recommendations

Ebola virus cause severe hemorrhagic fever with high percentage of fatal outcome in humans, and several

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species of non-human primates (NHPs). Human Ebola outbreaks usually occur abruptly from a vaguely defined source, with subsequent rapid spread from person to person. Ebola viruses are highly infectious and contagious. Understanding the clinical presentation, prompt diagnosis and suitable treatment are major steps towards the prevention of death and transmission of virus to other people. Generally the potential for global spread via transportation networks, large scale epidemic potential, given short incubation period, severity of illness and wide transmission patterns, potential for impact on non-human primate populations, limited treatment options and its concern for development as bioterrorism agents make the disease an economically important emerging disease being the hot issue for mass medias and different organizations. The fight against Ebola necessarily requires the global coordination of efforts between countries.

Based on the above conclusion the following recommenda tions are forwarded:

- Awareness should be created about the disease to prevent its spread and mitigate the disease.
- Individuals those are at high risk like Hunters, health professionals and those having contact with secretions should take appropriate care when handling animals or patients.
- Men infected with Ebola virus should not have sex for 3 months or until tests show that semen is free of the virus.
- Dead persons and animals should be buried appropriately to avoid potential source of infection.
- The global coordination of efforts between countries should be required to fight against Ebola virus disease.

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