Ebola Virus a Major Threat for Dental Professionals: A Review Article

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Ebola virus (EBOV) is the causative agent of lethal viral hemorrhagic fever. Since 1970, it has been found in sub-Saharan Africa. However, a current epidemic of 2014-2015, in West Africa, is caused by Zaire species of EBOV. This EBOV belongs to Filoviridae family. Term Filoviridae is derived from Latin word “Filum” meaning thread like based on its filamentous structure. Transmission of this virus can occur through various modes such as person to person, through animals and other routes. Person to person transmission occurs through direct contact with blood, body fluids, or skin of patients. Till date, there has been no reported case of transmission of the virus through saliva. However, some studies have confirmed the fact that all cases with detectable serum level of EBOV ribonucleic acid also show their level in saliva and also considering the fact that incubation period for all bodily fluids including saliva is 21 days. Thus, dental professionals are at risk of acquiring infection if infection control measures are not used. Hence, oral health care professionals should have a thorough knowledge about the oral manifestations of the disease to prevent life-threatening complications.

INTRODUCTION

Ebola virus (EBOV) belongs to Filoviridae family. Family has 2 members EBOV and Marburg virus. These 2 are among the most virulent pathogens in human. EBOV is a causative agent of lethal viral hemorrhagic fever. Since 1970, it has been found in sub-Saharan Africa. The current epidemic of 2014-2015, in West Africa, is caused by Zaire species of EBOV. EBOV disease (EVD) is a current threat and major concern for health care workers. Mildly symptomatic or asymptomatic carriers may seek dental treatment which can lead to transmission of disease through saliva. Therefore, oral health care professionals should have a thorough knowledge of sign symptoms and oral manifestation of the disease.

CLASSIFICATION AND STRUCTURE

Four virus families have been implicated to viral hemorrhagic fevers. Namely Arenaviridae, Bunyaviridae, Filoviridae, Flaviviridae. Among these EBOV belongs to Filoviridae family. Term Filoviridae is derived from Latin word “Filum” meaning thread like based on its filamentous structure. Filoviridae family has 2 members EBOV and Marburg virus. Genus EBOV has 5 species that includes Zaire, Sudan, Ivory coast, Bundibugyo, and Reston.¹ These are lipid enveloped, non-segmented ribonucleic acid (RNA) virus having 80 nm in diameter and length of 1.1 μm arranged in twisted pattern.² Viral genome consists of 7 genes. These include nucleoprotein, virion protein (VP) 35, VP40, glycoprotein, VP30, VP24, RNA-dependent RNA polymerase (L).³⁴ All the genes are monocstronic and encode for one structural protein except glycoprotein gene. Nucleoprotein associated with VP35, VP30, and RNA-dependent RNA polymerase to functional transcriptase - Replicase complex that encapsulate the inner ribonucleoprotein complex of virion particle.⁵ The additional functional role of VP 35, which is interferon antagonist, is present in ribonucleoprotein complex. VP40 serves as matrix protein while VP24 structural protein associated with membrane interferes with interferon signaling. Glycoprotein forms trimeric spikes consisting of glycoprotein 1 and glycoprotein 2 - two disulfide-linked furin-cleavage fragments.⁶

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Among the 5 members of EBOV only 4 cause disease in humans. First to be recognized causing disease in humans was Zaire virus, in the year 1976. The virus caused a multiple outbreaks in central Africa and also the current 2014-2015 epidemic in West Africa. Sudan virus has caused 4 epidemics 3 in Sudan, in 1976 and 2004, respectively; and 1 in Uganda, in 2000. Ivory coast caused disease in only 1 person and that survived but has been associated with marked decrease in number of ape population of Thai forest Bundibugyo caused an epidemic of EVD in Uganda in 2007.

**Epidemiology**

In 1967, the first case of hemorrhagic fever was reported in Germany. Causative was identified to be Marburg virus. Later on in the year 1976, 2 outbreaks occurred in Sudan and Zaire in this causative agent was identified from patients and was termed Ebola. Term Ebola was given after the name river. However, these two outbreaks were caused by different species of EBOV and were called Sudan EBOV and Zaire EBOV. In 3rd EBOV species was discovered from infected ethologist, in 1994, and was called Cote d'Ivoire EBOV. Rest of two species, that is, Bundibugyo and Reston EBOV were discovered from equatorial Africa and Philippines, respectively.

An epidemic of 2014-2015 began in West Africa nation of Guinea, in late, 2013. It was later confirmed by world health organization, in the year 2014. The first case was reported in a 2-year-old child who developed fever, vomiting, black stools but no hemorrhage. Later on epidemic spread to Liberia, Sierra, Leone, Nigeria, Senegal, and Mali.

**Reservoir and Transmission**

Fruit bats are the reservoir while humans are host species for EBOV. According to a study, by Towner et al., isolation of Marburg virus from bats of Uganda was done. However, only noninfectious EBOV have been detected from bats of central Africa. However, bats these are one of the reservoir hosts of EBOV, in Africa. However, the mystery lies in the fact that how did transmission of the virus occurred from bats to humans, in 2014-2015, outbreak of west Africa.

Transmission of the virus can occur through various modes such as person to person, through animals and other routes. Other routes include accidental infection of worker in biosafety level 4 facility where the virus is being studied or when virus has been used as biological weapon.

Person to person transmission through direct contact with blood, body fluids, or skin of patients with EVD, including those who have died from the infection.

**Transmission through Bodily Fluids**

Blood, feces, and vomit are considered to be most infectious agent according to WHO. However, detectable level of the virus has also been found in urine, semen, saliva, breast milk, tears, and sweat. Till date, there has been no reported case of transmission of the virus through saliva. In a study done by Formenty et al., on detection of EBOV in oral fluid confirmed the fact that all cases with detectable serum level of EBOV RNA also show their level in saliva. Moreover, also considering the fact that incubation period for all bodily fluids including saliva is 21 days; thus, dental professionals are at risk of acquiring infection if infection control measures are not used.

**Air Borne Transmission**

Aerosol transmission of EBOV has not been documented yet. Under experimental settings, there has been only one reported case of transmission of the virus in monkeys through the air. Therefore, dental professional may be at risk of developing the disease if exposed to aerosols produced during the ultrasonic scaling procedure.

**Through Contaminated Surfaces**

According to Centers for Disease Control and Prevention (CDC) virus on surfaces may remain infectious, from hours to days. However, by proper environmental cleaning risk of transmission can be reduced or rather eliminated.

**Nosocomical Transmission**

Whenever personal protective measures are not used properly, or they are not available in the remote areas transmission of the virus to health care worker may occur. Till date, no case has been reported of transmission of the virus in dental setting however many medical cases have been reported. A study was conducted in the year 2014 for 7 months, in Sierra Leone that included 3854 laboratory confirmed cases of viral hemorrhagic fever. The study showed that the incidence of Ebola in health care workers was 103 fold higher than that in general population.

**Transmission in Animals**

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PATHOGENESIS

Most of the data on pathogenesis of EBOV has been obtained from laboratory experiments on mice, guinea pigs, and non-human primates because of the fact that clinical studies cannot be performed in outbreaks. The virus can enter the host through the mucosal surface, break in continuity of epithelium, abrasion of the skin or parenteral introduction and also through direct contact with infected patients cadavers. The virus has an incubation period of 2-21 days. However, mean incubation period for Zaire species of EBOV that caused current epidemic of Africa is 6.3 days due to injection and 9.5 days for contact exposure. EBOV can infect wide variety of cells including monocyte, macrophages, dendritic cells endothelial cells, fibroblast, hepatocytes, adrenal cortical cells. Studies on non-human primates infected with EBOV experimentally have shown that monocyte, macrophages, and dendritic cell are early and preferred multiplication site for virus. Infection from these cells is spread to regional lymph nodes via lymphatic system and to liver and spleen via blood. Later on the dissemination of infection from spleen and lymph nodes to other tissues occurs by migration of monocytes, macrophages, and dendritic cells. These infected macrophages cannot mount interferon response, delays or obstructs the action of macrophages which initiates blood coagulation pathway. Furthermore, they cause the release of inflammatory proteins and nitric oxide. Increased production of nitric oxide is associated with pathological effects such as apoptosis of bystander lymphocytes, tissue damage, and loss of vascular integrity. Thus, loss of vascular integrity can lead to blood leakage. Along with this extrinsic coagulation pathway can be triggered by virus-infected macrophages that synthesize cell surface tissue factor. Furthermore, these macrophages are triggered by proinflammatory cytokines to produce tissue factor. Combination of these 2 factors can lead to rapid development and severe coagulopathy in Ebola infection. The effect of virus is also seen on other systems such as liver leading to dysregulation information of coagulation proteins, gastrointestinal tract leading to diarrhea, and vomiting which can in turn lead to acute volume depletion, hypotension, and shock. Because of uncontrolled virus replication and the ability of virus to effect a major organ of the body can lead to the death of a patient.

CLINICAL FEATURES

The incubation period is of 2-21 days. Abrupt onset of fever, chills, malaise, and myalgia occurs. On 5-7 days of illness exanthematos rash is noted that will later on desquamate in survivors. Conjunctivitis is also among the earliest and most frequent sign. Always seen bilateral and is reported in approximately 35-50% cases. Later on anorexia, nausea, vomiting, abdominal pain, diarrhea occurs because of involvement of gastrointestinal system. Respiratory system involvement leads to chest pain, shortness of breath, cough, and nasal discharge. Vascular and neurological manifestations include edema, postural hypotension, headache, confusion, and coma. During the peak of disease, hemorrhagic manifestations can be seen that include petechiae, ecchymosis, uncontrolled oozing from venipuncture site, mucosal hemorrhagic effusions. In later course of disease shock, delirium, coma develops.

ORAL MANIFESTATIONS

Gingival bleeding, mucosal lesions, and pain during deglutination are the most characteristic oral sign and symptom. Other sign includes epistaxis, bleeding from injection sites, rash, and conjunctivitis. These features are seen in early and mild form of the disease. Knowledge of these features can help dental professional to suspect the disease at early stages.

Gingival bleeding is seen along with other forms of bleeding such as epistaxis and bleeding from the injection site. Howsoever, bleeding is usually not seen in early or mild forms and is frequently associated with an advanced form of the disease. Thus, mild or asymptomatic EBOV patients visiting dental office may not show this sign.

Sore throat to severe dysphagia can occur as a result of edema and mucosal lesion. Some of the cases have been reported in the literature that shows that EBOV infected patients may have mucosal lesions such as white or red patch, aphthous such as ulcer and grayish exudative lesions. Ndambi et al. in the year 1999, reported a case of EBOV infected patient that showed gingival bleeding, mucosal redness, dysphagia, epistaxis, bleeding from injection site, conjunctivitis, and rash. Similary, another case was reported by Roddy et al., in the year 2002, demonstrating all similar features except mucosal redness. Because of the severity of disease at advanced stages dental care professional are unlikely to treat individuals who suffer from EVD. Howsoever, dental professional may come across mild or asymptomatic patients who are not aware of their disease. Reports suggest that in case of endemics 1-6% of healthy individuals and 3-9% of close family members are infected without themselves developing the disease.

Dental professional must be thorough enough to differentiate between EBOV infection and flu. After 5 days of infection, common features for both of these are sore throat, cough, and fatigue while along with those EBOV infection will have a rash. Within 8-10 days, symptoms of influenza begin.
to fade while, in EBOV high fever, conjunctivitis, loss of appetite, shortness of breath, and chest pain continues. These symptoms subside completely within 10 days for flu while continue and exaggerate in cases of Ebola infection.

LABORATORY DIAGNOSIS

Although these variables are less specific but are seen associated with Ebola hemorrhagic fever. These include early leukopenia with lymphopenia followed by neutrophilia, thrombocytopenia, highly raised serum aminotransferase level. Prothrombin time and partial thromboplastin levels are extended.

Measurement of host specific immune responses to infection and detection of viral particle in infected individuals is 2 main features for the diagnosis of the virus. Acute infection can be diagnosed with the help of reverse transcription polymerase chain reaction and antigen detection enzyme-linked immunosorbent assay (ELISA). From 3rd up to 7-16 days from onset of symptoms, viral antigen and nucleic acid can be detected in blood. Direct immunoglobulin G (IgG), IgM ELISA and IgM capture ELISA most commonly used assay for antibody detection. IgM antibodies appear 2 days post onset of symptoms and disappear between 30 and 168 days after infection while IgG specific antibodies are formed between 6 and 18 days and remains in blood till years.

A probable diagnosis of EBOV can be made based on rising IgM or IgG titre. Diagnosis of recent infection is made if IgM or increasing IgG titre are found.

TREATMENT AND PREVENTION

Till date, there has been no specific treatment or vaccine for EBOV. This is because the virus has highly glycosylated surface proteins and infects monocytes, macrophages, dendritic cells. Since health care worker are extremely susceptible to catching EVD from infected patients, for suspected workers immediate examination, isolation should be provided. The proper use of protective equipment should be made at risk of infection increase with increase in frequency of contact. Dental professional are constantly exposed to saliva and blood in daily routine procedures and therefore are at constant threat of acquiring the infection and thus standard infection control measures should be taken to prevent transmission of virus.

Recommendations given by the CDC and Prevention 2014 for prevention of EBOV transmission in health care workers include:

- The use of appropriate personal protective equipment that includes double gloves, disposable shoe cover
- Infection control measures should be followed properly
- Immediately notify officials if one has got direct contact with blood or body fluid of a person sick with Ebola virus
- Proper handling of needles, sharps, and safe infection practices
- Proper cleaning of contaminated surfaces.

If prevention methods fails, measures should be taken to control further transmission of the virus. These includes controlling the rodent population, use of insect repellent, bed nets, insect barriers, environmental decontamination with hypochlorite and phenolics, regular washing hands with soap and water.

CONCLUSION

In current scenario, EVD has been found to be a major threat to health professionals, not only in the EBOV endemic areas but also in Asian countries. Oral and dental health care providers are at a greater potential risk. One because the virus can be transmitted not only by blood but also by saliva, and two potentially contagious asymptomatic or mildly symptomatic individuals infected with EBOV can seek oral or dental care leading to its transmission. Proper knowledge of the disease helps in its early diagnosis, and scrupulous use of infection control measures are probably enough to minimize such a risk.

REFERENCES


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