Introduction

Ebola, earlier termed as Ebola hemorrhagic fever (EHF), is a critically lethal ailment which primarily affects the humans and nonhuman primates. Ebola virus disease (EVD) occurs due to a virus infection which belongs to the family Filoviridae and genus Ebolavirus. EVDs has posed diagnostic challenges and has been a universal public health threat since its discovery. While investigating an alleged yellow fever case, Dr. Peter Piot in the year 1976 first detected the disease in Zaire, Africa (presently the Democratic Republic of Congo). The name “Ebola” was termed as the disease was noticed near the Ebola river in Congo.

Fruit bats of Pteropodidae family, such as Hypsignathus monstrous, Epomops franqueti, and Myonycteris torquata serve as the natural hosts of the EBOV in Africa. Nonhuman primates may develop the infection by eating the partly eaten fruits and may also transmit the infection to humans.

Ebola virus disease (EVD), a fatal viral hemorrhagic illness, is due to infection with the Ebola virus of the Filoviridae family. The disease has evolved as a global public health menace due to a large immigrant population. Initially, the patients present with nonspecific influenza-like symptoms and eventually terminate into shock and multiorgan failure. There exists no specific treatment protocol for EVD and only supportive and symptomatic therapy is the line of treatment. This review article provides a detailed overview of the Ebola virus; it’s clinical and oral manifestations, diagnostic aids, differential diagnosis, preventive aspects, and management protocol.

Keywords: Ebola virus, oral manifestations, public health menace, symptomatic therapy

Abstract

Ebola virus disease (EVD), a fatal viral hemorrhagic illness, is due to infection with the Ebola virus of the Filoviridae family. The disease has evolved as a global public health menace due to a large immigrant population. Initially, the patients present with nonspecific influenza-like symptoms and eventually terminate into shock and multiorgan failure. There exists no specific treatment protocol for EVD and only supportive and symptomatic therapy is the line of treatment. This review article provides a detailed overview of the Ebola virus; it’s clinical and oral manifestations, diagnostic aids, differential diagnosis, preventive aspects, and management protocol.

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Introduction

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and symptomatic therapy, along with monitoring coagulopathies and multiorgan dysfunction.[2]

The World Health Organization (WHO) affirmed the EVD outbreak as a “Public Health Emergency of International Concern” on August 8th, 2014.[3]

With the enormous immigrant population, India is estimating the likelihood of a probable EVD outbreak. The Ministry of Health and Family Welfare, Government of India, in collaboration with other agencies has appraised the situation and recommended travel instructions by air, land, and sea and health care professionals.[11]

**Taxonomy**

The virus belongs to the *Ebola virus* genus, *Filoviridae* family, and *Mononegavirales* order.[12] The genus *Ebolavirus* includes the following species—Zaire ebolavirus (EBOV), Reston ebolavirus (RESTV), Bundibugyo ebolavirus (BDBV), Tai Forest ebolavirus (TAFV), Sudan ebolavirus (SUDV), and the newly identified Bombali ebolavirus (BOMV).[13] Except for exclusive identification of RESTV in the Philippines, all the other species causes endemic West African EVD.[14]

EBOV responsible for the EHF causes the highest human mortality (57%–90%), followed by SUDV (41%–65%) and Bundibugyo virus (40%). TAFV has caused only two nonlethal human infections to date, whereas RESTV causes asymptomatic human infections.[15]

Figure 1 shows the taxonomy of Ebola virus.

**Transmission**

Based on the Centers for Disease Control and Prevention (CDC) classification, Ebola virus is considered as a biosafety level 4 and category A bioterrorism pathogen with an immense likelihood for massive nationwide transmission.[16]

**Source of Infection**

Intimate physical contact with the patients in the acute disease stages and contact with the blood/fluids from the dead individuals constitutes the most important modes of transmission.[17]

The long-established funeral ceremonies in the African countries entail direct handling of the dead bodies, thus significantly contributing to the disease dissemination. Unsafe conventional burial procedures accounted for 68% infected cases in 2014 EVD outburst of Guinea.[18]

EBOV RNA may be identified for up to a month in rectal, conjunctival, and vaginal discharges and semen specimens may demonstrate the virus presence up to 3 months, thus signifying the presence of EBOV in recuperating patients.[19] The sexually transmitted case of EVD has been reported between a convalescent patient and close family member. Another study demonstrated a case in a recuperating male patient. The patient’s semen specimen tested positive with Ebola viral antigen almost 3 months after the disease onset.[20]

Asymptomatic EBOV carriers are not infectious and do not have a major role play in the EVD outburst, and the field practice in Western Africa supported this assumption.[21] However, this presumption was refuted after the documentation of a pioneer asymptomatic carrier case in North Gabon epidemic (1996).[22]

EBOV has been detected from blood, saliva, semen, and breast milk, while RNA has been isolated from sweat, tears, stool, and on the skin, vaginal, and rectal swabs, thus highlighting that exposure to infected blood and bodily secretions constitute the major means of dissemination.[23]

Eating uncooked infected animal meat such as bats or chimpanzees account significantly to oral EVD transmission, especially in the African countries.[24] The demonstration of the Ebola virus in the Filipino pigs in 2008 triggered the likelihood of an extensive range of possible animal hosts.[25]

EVD dissemination has also been reported with hospital-acquired infections, particularly in areas with poor hygiene conditions. The infected needles usage was responsible for the 1976 EVD outbreak in Sudan and Zaire.[26,27] Improper hygiene and sterilization were the crucial factors for the 1967 Yambuku EVD outburst.[27]

EVD dissemination may also occur through the inanimate materials with infected body secretions (fomites).[28] However, disease transmission through the airborne and droplet infection is ambiguous.[10]

Figure 2 shows the primary and secondary transmission of disease.

Table 1 depicts the possible routes of transmission.

**Epidemiology**

The vast majority of EVD cases and outbursts have been endemic to African continent ever since the disease detection.
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Table 1: Possible routes of transmission

| Mode of transmission            | Consensus likelihood of occurring | Known facts                                                                 | Unknown facts                                                                                   |
|---------------------------------|------------------------------------|-----------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| Airborne/aerosol (small droplet/droplet nuclei) | Unlikely from epidemiology of disease | EBOV can be aerosolized mechanically and cause lethal disease in nonhuman primates at low concentrations. Outbreaks contained without airborne precautions in the affected population. EBOV detected after 90 min in experimental small aerosols. | Ability of the virus to become airborne through respiratory tract in humans and animals. Airborne stability of EBOV in tropical climates. Whether aerosol generating procedures (AGPs) produce EBOV aerosols that cause transmission |
| Fomites                         | Less likely from environmental sampling | Virus found in dried blood Persists on glass and in the dark for 5.9 days | EBOV stability in tropical climates and on surfaces Whether infectious fluids are formed into droplets by humans Range of droplets containing EBOV |
| Droplet (large droplet)         | Likely from epidemiology and experiments | EBOV found in stool, semen, saliva, breast milk Accidental infections in nonhuman primates, possibly from power washing EBOV infections without direct contact | |
| Bodily fluids contact           | Very likely from epidemiology and experimental data | Sharing needles and handling the deceased or sick are high risk factors How much virus is shed in different fluids | |

Figure 2: Primary and secondary transmission

in 1976 and 36 such outbreaks have occurred in six African countries.

Table 2 shows Ebola epidemiological outbreaks between 1976 and 2014.

The 2014–2016 EVD started in South East Guinea rural surroundings and eventually became a global public health menace by rapidly disseminating to urban localities and other countries.

Figure 3 depicts the geographical distribution of Ebola virus disease.

The conducive environmental surroundings of the African continent facilitate EVD endemicity. However, intermittent imported Ebola cases have also been noticed in United States, United Kingdom, Canada, Spain, and Thailand.

Figure 4 depicts the distribution of Ebola virus disease in West African Countries.

Out of the unparalleled globally reported 28,616 cases and 11,310 casualties, Liberia accounted for almost 11,000 cases and over 4,800 deaths.

Table 3 shows the statistics of the 2014–16 West African outbreak.

Pathogenesis

Ebola viruses penetrate the human body through mucous membranes, skin lacerations/tear, close contact with infected patients/corpse, or by direct parental dissemination. EBOV has a predilection to infect various cells of immune system (dendritic cells, monocytes, and macrophages), endothelial and epithelial cells, hepatocytes, and fibroblasts where it actively replicates by gene modulation and apoptosis and demonstrate significantly high viremia. The virus reaches the regional lymph nodes causing lymphadenopathy and hematogenous spread to the liver and spleen promote an active inflammatory response. Release of chemical mediators of inflammation (cytokines and chemokines) causes a dysregulated immune response by disrupting the vasculature system harmony, eventually causing disseminated intravascular coagulation and multiple organ dysfunction.

Figure 5 demonstrates the pathogenesis of Ebola virus disease.

Clinical Features

Due to the bizarre and atypical manifestations in the initial phase, mimicking dengue fever, typhoid fever, malaria,
### Table 2: Ebola outbreaks between 1976 and 2014 (Adapted from WHO 2014)

| Year | Country/village | Ebola virus subtype | Number of human cases | Number of deaths | Mortality | Source and spread infection |
|------|-----------------|---------------------|-----------------------|-----------------|-----------|---------------------------|
| 1976 | Sudan, Nzara and Marida | Sudan virus | 284 | 151 | 53% | Close contact within hospitals, infecting many hospital staff |
| 1976 | Zaire, Yambuku | Ebola virus | 318 | 280 | 88% | Contaminated needles and syringes in hospitals |
| 1976 | England | Sudan virus | 1 | 0 | | Laboratory infection; accidental stick of contaminated needles |
| 1977 | Zaire, Tandala | Sudan virus | 1 | 1 | 100% | Noted retrospectively |
| 1979 | Sudan, Nzara and Marida | Sudan virus | 34 | 22 | 65% | Recurrent outbreak at the same site as 1976 |
| 1989 | USA, Virginia, Pennsylvania | Reston virus | 0 | 0 | | Ebola virus was introduced in to quarantine facility by monkeys from the Philippines |
| 1989-1990 | Philippines | Reston virus | 3 | 0 | | Source: Macaques from USA. Three workers (animal facility) developed antibodies, did not get sick. |
| 1990 | USA, Virginia | Ebola virus | 4 | 0 | | The same to 1989 |
| 1994 | Gabon | Ebola virus | 52 | 31 | 60% | Initially thought to be yellow fever; identified as Ebola in 1995 |
| 1994 | Cote d’Ivoire | Tai forest virus | 1 | 0 | | Scientist became ill after autopsy on a wild chimpanzee (Tai Forest) |
| 1995 | Democratic Republic of Congo (Zaire) | Ebola virus | 315 | 250 | 81% | Case-patient worked in the forest; spread through families and hospitals |
| 1996 | Gabon | Ebola virus | 37 | 21 | 57% | Chimpanzee found dead in the forest was eaten by hunters; spread in families |
| 1996-1997 | Gabon | Ebola virus | | | | Case-patient was a hunter from forest camp; spread by cloth contact |
| 1996 | South Africa | Ebola virus | 2 | 1 | 50% | Infected medical professional travelled |
| 1996 | Russia | Ebola virus | 1 | 1 | 100% | Laboratory contamination |
| 2000-2001 | Uganda | Sudan virus | 425 | 223 | 53% | Providing medical care to Ebola case-patient without using adequate personal protection measures |
| 2001-2002 | Gabon | Ebola virus | 65 | 53 | 82% | Outbreak occurred over border of Gabon and Republic of Congo |
| 2001-2002 | Republic of the Congo | Ebola virus | 57 | 43 | 75% | Outbreak occurred over border of Gabon and Republic of Congo |
| 2002-2003 | Republic of the Congo | Ebola virus | 143 | 128 | 89% | Outbreaks in the district of Mboma and Kelle in Cuvette Quest Department |
| 2003 | Republic of the Congo | Ebola virus | 35 | 29 | 83% | Outbreaks in the villages of Mboma district, Cuvette Quest Department |
| 2004 | Sudan, Yambia | Sudan virus | 17 | 7 | 41% | Outbreak concurrent with an outbreak of measles, and several cases were later reclassified as measles |
| 2004 | Russia | Ebola virus | 1 | 1 | 100% | Laboratory infection |
| 2007 | Democratic Republic of the Congo | Ebola virus | 264 | 187 | 71% | The outbreak was declared on November 20. Last death on October 10 |
| 2007-2008 | Uganda | Bundibugyo virus | 149 | 37 | 25% | First reported occurrence of a new strain |
| 2008 | Philippines | Reston virus | 6 | 0 | | Six pig farm workers developed antibodies; did not become ill |
| 2008-2009 | Democratic Republic of the Congo | Ebola virus | 32 | 15 | 47% | Not well identified |
| 2011 | Uganda | Sudan virus | 1 | 1 | 100% | The Uganda Ministry of Health informed the public that a patient with suspected Ebola died on May 6th 2011 |
| 2012 | Uganda, Kibuale | Sudan virus | 11 | 4 | 36% | Laboratory tests of blood samples were conducted by UVRI and CDC |
| 2012 | Democratic Republic of the Congo | Bundibugyo virus | 36 | 13 | 36% | This outbreak has no link to the contemporaneous Ebola outbreak in kibaale, Uganda |
| 2012-2013 | Uganda | Sudan virus | 6 | 3 | 50% | CDC assisted the ministry of Health in the epidemiology and diagnosis of the outbreak |
| 2014 | Democratic Republic of the Congo | Zaire virus | 66 | 49 | 74% | The outbreak was unrelated to the outbreak of West Africa |

UVRI: Uganda Virus Research Institute; CDC: Centers for Disease Control and Prevention
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meningococcemia, and other bacterial infections, EVD poses diagnostic dilemmas.\[37\]

The incubation period ranges from 2 to 21 days. However, symptoms usually develop 8–11 days following infection.\[38,39\]

The initial disease phase is represented by constitutional symptoms.\[38\] High-grade fever of >38°C is the most frequently reported symptom (85–95%), followed by other vague symptoms such as general malaise (85–95%), headaches (52–74%), dysphagia, sore throat (56–58%), and dry cough.\[41,42\] The progressively advanced disease is accompanied by abdominal pain (62–68%), myalgia (50–79%), nausea, vomiting, and diarrhea (84–86%).\[41\]

Variety of hemorrhagic manifestations forms an integral component of the late disease phase.\[38\] Gastrointestinal tract bleeding manifests as petechiae, hematuria, melena, conjunctival bleeding, contusion, or intraperitoneal bleeding. Mucous membrane and venipuncture site bleeding, along with excess clot formation may also occur. As the features advances with time, the patients experience dehydration, confusion, stupor, hypotension, and multiorgan dysfunction, resulting in fulminant shock and ultimately death.\[43,44\]

Maculopapular exanthema constitutes a characteristic manifestation of all Filovirus infection, including EVD.\[45\] The rash usually appears during the 5th to 7th day of disease and occur in 25–52% of patients in the past EVD outbreaks.\[46\]

Table 4 shows the clinical manifestations of Ebola virus disease.

Although EVD has a number of similar features with other viral hemorrhagic fevers (e.g. dengue), there are differences that set them apart.

Table 5 depicts the differentiating features of the Ebola virus and dengue virus infection.

**Orofacial features**

Gum bleeding, atypical mucosal lesions, and odynophagia comprise the distinctive oral manifestations. Epistaxis

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**Figure 3:** Geographic distribution of Ebola virus disease outbreaks

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| WHO report date | Guinea total cases | Guinea total deaths | Liberia total cases | Liberia total deaths | Sierra Leone total cases | Sierra Leone total deaths | Total cases | Total deaths |
|-----------------|-------------------|-------------------|-------------------|-------------------|-------------------------|-------------------------|-------------|-------------|
| 13th APRIL 2016 | 3814              | 2544              | 10678             | 4810              | 14124                   | 3956                    | 28616       | 11310       |

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**Table 4:** Clinical manifestations of Ebola virus disease

| Days | Phase       | Main features                                      | Other features                                      |
|------|-------------|----------------------------------------------------|----------------------------------------------------|
| O-3  | Early febrile | Fever                                              | Malaise, fatigue, body ache                        |
| 3-10 | Gastrointestinal | Epigastric pain, nausea, vomiting, diarrhoea     | Persistent fever, headache, conjunctival injection, abdominal and chest pain, arthralgia, myalgia, hiccupus, delirium |
| 7-12 | Shock or recovery | Shock: diminished consciousness or coma, Rapid thread pulse, oligaemia, anuria, tachypnea | Recovery                                           |
| ≥ 10 | Late complications | Gastrointestinal hemorrhage                  | Resolution of gastrointestinal symptoms, increased appetite, increased energy. |
|      |              |                                                    | Secondary infections: oral/esophageal candidiasis, persistent neurocognitive abnormalities |
(nasal bleed), bleeding from venipuncture sites, conjunctivitis, and cutaneous exanthema are the other manifestations. Bleeding tendencies and gum bleeding is not seen in asymptomatic or initial EBOV patients reporting to the dental hospital.

EVD dissemination in the field of oral and dental health may appear nonsignificant; although, probable situations which may pose a risk to dental health professional have been appraised by Samaranayake et al. and Galvin et al.

Table 6 depicts the various orofacial manifestations of Ebola virus disease

### Diagnosis

EVD patients usually demonstrate altered laboratory parameters based on the stage of the disease.

Table 7 shows the laboratory findings in Ebola virus disease.

The WHO (2014) recommended the sample collection of whole blood or oral swab at suitable centres called Ebola treatment centers. Reverse transcriptase polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay (ELISA) are the most frequently utilized tests for laboratory affirmation of the EVD. RT-PCR is capable of detecting viral RNA in the blood samples of infected patients immediately after the commencement of signs and symptoms, has a high sensitivity (up to 100%), and gives results within 1–2 days in cases of epidemics. ELISA detects the immunoglobulins G and M in samples of infected patients, has a low sensitivity (91%) and is not suitable for initial affirmation during an outbreak.

### Prevention

The most imperative strategy in EVD is to avert the vulnerable population from getting infected and limit the transmission. These preventive strategies entail intensive and rigorous endeavors from the Government, public health amenities, medical units, and personals.

The most essential aspect to curb EVD transmission is to avert direct bodily contact with infected individuals and their body fluids.

Health caregivers are extremely vulnerable and experience an augmented professional threat for EVD. Thus, scrupulous adherence to the universal infection control measures is fundamental in all the hospitals, laboratories, and other health care services. The U.S. CDC has advocated the appropriate use of various personal protective equipment as a mandate for health care professionals.

The risk of rapid importation of Ebola virus into human beings can be prevented by averting the direct bush meat and bats contact.

Unsafe traditional burial procedures, especially in the African continent significantly contributed to the EVD transmission. Hence, it is essential to practice safe and guarded funeral rituals to prevent the disease spread.

WHO recommends the implementation of safe sex practices to combat the sexual transmission of EVD. Strict abstinence or proper and regular condom use in male EVD survivors at least for a period of 12 months of the symptom onset or until their semen has twice tested negative should be followed.

Dental health care personals are extremely susceptible to EVD as they are in regular contact with blood and saliva during the routine diagnostic procedures. There is no documented case of EVD through saliva till date. A study on the identification of EBOV in oral fluids affirmed that patients presenting with demonstrable serum levels of EBOV RNA also exhibit identifiable salivary levels. The incubation period for all body
fluids including saliva is 21 days; hence, oral health personals are vulnerable to develop the disease if universal infection control protocol is not followed.\textsuperscript{[58]}

Table 8 demonstrates the various infection control measures to prevent the Ebola virus spread.

Box 1 shows the travel guidelines to EBOV affected regions.

| Differentiating features | Dengue | Ebola |
|--------------------------|--------|-------|
| Incubation period        | 3-14 days | 2-21 days |
| Etiology                 | RNA virus belongs to the genus \textit{Flavivirus} of family \textit{Flaviviridae} | RNA virus belongs to the genus \textit{Ebola} virus of family \textit{Filoviridae} |
| Mode of transmission     | Arthropod borne | Direct contact with infected blood/body fluids and environment contaminated with these secretions |
| Human-human transmission | No | Yes |
| Mortality                | 0.04%-0.05% | 50%-90% |
| Typical signs and symptoms | Common |
| Fever | Common | Common |
| Headache | Common and high intensity (usually retrobulbar) | Common and high intensity |
| Muscle ache and pain | Common and severely intense (known as break bone fever) | Common |
| Nausea and vomiting | Common |
| Ocular involvement | Nonpurulent conjunctivitis | Conjunctival injection; subconjunctival hemorrhage |
| Diarrhea | Uncommon |
| Bleeding | Unusual |
| Rash (maculopapular exanthema) | Moderately elevated; initial rash occurs before or during 1-2 days of fever; 2nd rash is seen 3-5 days later | Elevated; occurs during the 5$^{th}$-7$^{th}$ day |
| Neurologic complications | Encephalitis | Persistent neurocognitive abnormalities |
| Course of disease | Dengue can be divided into undifferentiated fever, dengue fever, and dengue hemorrhagic fever. | Features can be divided into 4 main phases: Early febrile phase, gastrointestinal phase, shock or recovery phase and late complications |
| Oral manifestations | Erythema, crusting of lips, and tongue and soft palatal vesicles are the prominent oral features. Hemorrhagic bullae, petechiae, purpura, ecchymoses, and bleeding gums may also be seen | Gingival bleeding, mucosal lesions, and pain during deglutination (odynophagia) are the most characteristic oral signs and symptoms. |
| Typical blood abnormalities | Platelets | Low | Low |
| Hematocrit | High | Low |
| Hemoglobin | High | Low |
| Aspartate transferase | Elevated | Elevated |
| INTERVENTIONS TO CONTROL THE SPREAD AND DISSEMINATION | Control of the vectors and their breeding sites | Avoid direct contact with the infected blood/body fluids and adopting universal infection control measures |
| TREATMENT | Supportive | Supportive |
| VACCINE DEVELOPMENT | In progress | In progress |

Box 1: Shows the UK Travel guidelines to EBV infested regions.

- Do not handle dead animals or their raw meat
- Avoid contact with patients who have symptoms
- Avoid unprotected sex with people in risk areas
- Wash fruit and vegetables before eating them
- Wash hands frequently using soap and water

Till date, there is no precise antiviral management or vaccination for EVD.\textsuperscript{[51]} The management protocol mainly relies on supportive and symptomatic therapy. Public health strategies emphasizing on epidemiological surveillance, contact tracing, and quarantine of the patient have been recommended to combat the dissemination of EVD.\textsuperscript{[59]}

Rehydration, adequate nourishment, analgesics, and blood transfusion form a keystone supportive treatment of EVD.
Table 6: Orofacial manifestations of Ebola virus disease

| Authors, Year | Oral bleeding | Oral mucosal lesions | Odynophagia | Other bleeding sites | Other features |
|---------------|---------------|----------------------|-------------|----------------------|---------------|
| Anonymous, 1978a | Gingival bleeding (48%) | Dry oral cavity | Painful throat (sensation of dry rope in the throat) (63%) | Epistaxis | Conjunctivae slightly injected but nonicteric |
| Anonymous, 1978b | | Small aphthous like ulcers | | | |
| Piot, 1978 | | | | | |
| | | Posterior pharynx slightly injected | | | |
| | | Fissures and open sores of the lips and tongue | | | |
| | | Oral throat lesions (73%) | | | |
| | | Fissures on the lips | | | |
| | | Herpetic oral lesions | | | |
| | | Grayish exudative patches on soft palate and oropharynx | | | |
| Sureau PH 1989 | Gingival and oral bleeding | Oropharyngeal bleeding ulcerations in the mouth and in the lips | Sore throat (32%) | Epistaxis | Hemorrhagic conjunctivitis |
| Bonnet, 1998 | Diffuse bleeding in the oral cavity (gums & tongue) | Oral thrush like lesions | Not reported | Bruses and bleeding at the injection sites (late stages) | Exanathematous rash on trunk |
| Bwaka, 1999 | Not reported | Not reported | Odynophagia | Injection sites (5%) | Conjunctival injection (47%) |
| Ndanbi, 1999 | Gingival bleeding (30%) | Oral/mucosal redness (30%) | Dysphagia (48%) | Epistaxis (4%) | Conjunctivitis (78%) |
| | | | | Injection site (30%) | |
| Mupere, 2011 | Not reported | Sore throat (10%) | Epistaxis (10%) | Conjunctival injection (40%) | |
| Korepeter, 2011 | Not reported | Pharyngeal Aрыthema | Sore throat | Bleeding from injection/venepuncture site | |
| Roddy, 2012 | Gingival bleeding (4%) | Not reported | Dysphagia (58%) | Epistaxis (8%) | Conjunctivitis (50%) |
| Chertow, 2014 | Not reported | Oral ulcers and Thrush | Throat pain | Not reported | Rash (12%) |
| WHO Ebola response team, 2014 | Bleeding gums (2.3%) | Not reported | Dysphagia (32.9%) | Unexplained bleeding (18%) | |
| | | | Sore Throat (21.8%) | Epistaxis (1.9%) | |
| | | | | Injection site (2.4%) | |

Table 7: Laboratory findings in Ebola virus disease

| Timing | Common laboratory findings |
|--------|---------------------------|
| Early illness | Leukopenia, lymphphenopenia, and thrombocytopenia |
| | Elevated hemoglobin and hematocrit |
| | Elevated aspartate aminotransferase and alanine aminotransferase (ratio≥3:1) |
| | Elevated prothrombin time, activated partial thromboplastin time, and D-dimer |
| Peak illness | Leukocytosis, neutrophilia, and anemia |
| | Hyponatremia, hypo- or hyperkalemia, hypomagnesemia, hypocalcemia, hyperalbuminemia, hypoglycaemia |
| | Elevated creatine phosphokinase and amylase |
| | Elevated blood urea nitrogen and creatinine |
| | Elevated serum lactate and low serum bicarbonate |
| Recovery | Thrombocytosis |
Intravenous fluids and oral rehydration solution endow with proper electrolytes substitute and maintain the intravascular volume. Unrelenting vomiting and diarrhea are taken care of by the use of antiemetics and antidiarrheal drugs. Suspected cases of secondary bacterial infections and septicemia are best managed by the use of prophylactic antibiotic regimen (third generation I.V. cephalosporins). Concurrent parasitic coinfections may also be seen and require prompt investigations and management.

Table 9 shows experimental treatment for Ebola virus disease.

A number of investigative clinical trials emphasizing on the development of vaccine, antibody therapies, and antiviral drugs have been conducted for EVD. Various clinical trials in Africa, Europe, and the United States suggest that Ebola vaccines are in various development stages (Phase I–III). A number of candidate vaccines employ diverse platforms, including recombinant viral vectors (most evolved vaccine candidate), DNA vaccines, inactivated viral particles, subunit proteins, recombinant proteins, and virus-like particles. Example of viral vectors expressing ebolavirus glycoproteins include recombinant simian adenovirus (cAd3), recombinant vaccinia virus, recombinant human adenovirus (Ad26), and a live vesicular stomatitis virus used alone or in prime-booster regimens.

However, Ebola virus having the glycosylated surface proteins and preferentially infecting the immune cells impedes the development of an effective vaccine.

**Dental Management**

Dental health care professionals in Europe have not encountered a case of EVD so far. However, health care personals (including dental surgeons) are more prone to EVD while treating patients in West or sub-Saharan Africa. Dental professionals are more likely to encounter asymptomatic EVD patients or those with early-stage vague symptoms.
Table 9: Experimental treatment for Ebola virus disease

| Drug                          | Drug type                              | Mechanism of action                                                                 | Ebola virus clinical trial phase | Result/status                                                                 | Other clinical trials                                                                 |
|-------------------------------|----------------------------------------|-------------------------------------------------------------------------------------|---------------------------------|-------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| FAVIPIRA VIR (T-705) (Fujifilm Holding Corp) | Nucleotide analogue and viral RNA polymerase inhibitor | Prevents viral replication by RNA chain termination and/or lethal mutagenesis      | Phase II (NCT02329054); JIKI; NCT02662855; Sierra Leone) | Efficacy in patients with low to moderate levels of virus | Administered with ZMapp to a patient who recovered; administered to a patient with convalescent plasma who recovered; retrospective study indicated increased survival and lower viral loads. |
| BCX4430 (BioCryst Pharmaceuticals Inc., Durham, NC) | Synthetic adenosine analogue | Inhibits viral RNA polymerase and results in RNA chain termination | Phase I (NCT02319772) | Phase I complete; results not available yet | Not Applicable                                                                 |
| TKM-Ebola (Tekmira Pharmaceutical Corp.) | Small Interfering (si) RNA agents with si RNA-Ebola virus specific compound | Gene silencing                                                                             | TKM-100802                      | Terminated              | Terminated early; did not demonstrate efficacy [77]; development has been suspended |
| Brincidofovir CMX001 (Chimerix Durham, NC) | Nucleotide analogue | Inhibits viral replication by inhibiting DNA polymerase                              | Phase II (NCT02271347)          | Terminated due to low enrollment; not currently under further development as EBOV therapeutic agent | Administered to 5 patients during the outbreak, often in combination with other therapies |
| AVI-6002 | Small Interfering (si) RNA agents Phosphoro-diamidate morpholino oligomer Ebola virus specific compound | Gene silencing                                                                             | Phase I (NCT01353027; NCT01593072) | Viable safety and tolerability    | Not Applicable                                                                 |
| AVI-7537 | Small Interfering (si) RNA agents Phosphoro-diamidate morpholino oligomer Ebola virus specific compound | Gene silencing                                                                             | Phase I (NCT01353027; NCT01593072) | Viable safety and tolerability    | Not Applicable                                                                 |
| Z-Mapp (Mapp Pharmaceuticals) | Combination of 3 different monoclonal antibodies-Ebola specific compound | Virus neutralisation                                                                        | Phase II (NCT02636322)          | Inconclusive efficacy due to insufficient statistical power | Administered to patients during the outbreak, often in combination with other therapies |
| JK-05 (Sihuan Pharmaceutical Holdings Group Ltd and Academy of Military Medical Sciences (Beijing, China)) | Broad spectrum antiviral drug | Inhibits viral RNA polymerase                                                          | Not Applicable                   | Not Applicable                                                              | Not Applicable                                                                 |
| Convalescent plasma or blood | Derived from surviving or cured Ebola patients contains anti Ebola antibodies | Phase I/II; NCT02333578 Phase II/III (NCT02342171; ISRCTN13990511) | Completed; results from one study found no improvement in efficacy in treated group | Whole blood: 1995 Kikwit outbreak—7 out of 8 survivors; administered to patients during the outbreak, often in combination with other therapies | Administered to a newborn in combination with ZMapp and buffy coat transfusion; patient survived |
| GS-5732 | Small molecule monophosphoramidate prodrug of an adenosine analogue | Inhibition of RNA-dependent RNA polymerase                                               | Phase I                          | Phase I complete; Phase II for efficacy in survivors with viral persistence in semen (NCT02818582) | Results not yet released                                                        |
| IFN-β | Cytokine family member | Inhibits the viral infection by activating the innate and adaptive immune response     | Phase I/II (ISRCTN17414946)         | Not Applicable                                                              | Not Applicable                                                                 |

Contd...
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Individuals with a travel history to Ebola endemic regions, but with no direct intimate contact with the disease fall in the low-risk category and may undergo any medical/dental health care procedures without restrictions. However, all the nonessential procedures should be postponed for 21 days in individuals with direct exposure to the virus. The regional Health Service Executive Department of Public Health needs to be notified when the exposed patient's treatment cannot be deferred or controlled with pharmacotherapy.\footnote{10}

Conclusion

EVD has emerged as a significant global public health menace due to multiple disease outbreaks in the last 25 years. Recent advancements are being carried out in the form of effective Ebola virus vaccine and anti-Ebola virus drugs. However, rapid geographic dissemination, nonspecific clinical presentation, lack of vaccine, and specific diagnostic test are the possible challenges to combat this dreaded public health menace.

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Conflicts of interest

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