Ebola virus disease – An Overview of the 2014 Outbreak in West Africa (up-to-end of 7 December 2014)

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ABSTRACT

In this article presented are the basic known findings on Ebola virus disease (EVD) from the current outbreak in West Africa 2014. As per World Health Organisation (WHO) data, from the first reported cases on 23 March 2014 in Guinea up to the end of 7 December 2014, the total number of reported EVD cases is 17,942 (confirmed, suspect and probably) with 6,388 deaths. The three most affected countries are: Guinea, Sierra Leone and Liberia reported 17,908 with 6,373 deaths. Over the four decade - from the first described Ebola virus diseases - EVD (formerly Ebola haemorrhagic fever) in two parallel outbreaks: first in Southern Sudan, subsequently in northern part of Democratic Republic of Congo (DRC) (formerly Zaire) 1976, there have been 23 outbreaks of Ebola virus disease in humans across Africa. The viruses isolated from the patients in the current West Africa outbreak most likely diverged from central African lineages around 2004, crossed from Guinea to Sierra Leone in May 2014, and has exhibited sustained human-to-human transmission subsequently, with no evidence of additional zoonotic sources. The WHO Ebola Response team concluded that the clinical course of infection according to clinical characteristics of patients in the previous EVD outbreaks is similar. There is currently no specific vaccine or medications (such as antiviral drugs) that have been proven to be effective in treating Ebola, but two vaccine candidates currently being tested in humans.

Key words: Ebola virus disease (EVD) epidemiology, outbreak, clinical features, diagnostics, treatment, prevention, control measures

BACKGROUND ON THE 2014 OUTBREAK

Ebola virus disease - EVD (formerly known as Ebola haemorrhagic fever) - wildly named today as Ebola, is severe, acute, often fatal disease of humans and non-human primates (such as monkeys, gorillas, and chimpanzees). From wild animals the virus is transmitted to people and it spreads in the human population through human-to-human transmission. During the current outbreak of Ebola in West Africa according to World Health Organisation (WHO) data, from the first reported cases 23 March 2014 in Guinea up to the end 7 December 2014, total of reported EVD cases is 17,942 (confirmed, suspect and probably) with 6,388 deaths. The average of EVD case fatality rate in this epidemic is around 50% and depending of outbreaks in past have varied from 25% to 90% [1].

After the first reported cases, epidemic spread rapidly across the border of Guinea to neighbouring countries Sierra Leone and Liberia; by plane (only one passenger) to Nigeria, and by land (one passenger as well) to Senegal. Mali reported the first case of Ebola virus diseases on 23 October 2014. Until today, the cases of EVD have been reported in: Guinea, Liberia, Mali, Sierra Leone, the United States of America, Nigeria, Senegal and Spain. The later three countries declared free of cases, as there were no new cases of EVD for the period of two maximum incubation (42 days) on the following dates: Senegal 17 October 2014, Nigeria 22 October and Spain 2 December 2014 [2].

On the 8 August 2014 WHO Director-General declared the current outbreak of Ebola in West Africa a Public Health Emergency of International Concern [3].

The three most affected countries are: Guinea, Sierra Leone and Liberia. These countries common findings are: cases are predominantly from large rural areas, but coming from major cities and capitals as well, with
present weakness of the health system (e.g. lacking of human and infrastructure resources for major epidemic control and establishing effective control measures) - recently emerged from a long period of conflict and instability. Therefore, all three countries facing enormous challenges in implementing control measures at the scale required to stop transmission and to provide clinical care for all persons with EVD [3].

Of all EVD reported cases, these three countries have been reported 17,908 with 6,373 deaths (the case fatality rate in all reported cases with a recorded definitive outcome is 76%, in hospitalized patients the case fatality rate is 61%). Reported case incidence is slightly increasing in Guinea, declining in Liberia, and may still be increasing or stable in Sierra Leone (Figure 1) [2].

![Map of West Africa showing geographical distribution of new and total confirmed and probable* cases in Guinea, Liberia, Mali, and Sierra Leone](image)

Figure 1.: Geographical distribution of new and total confirmed and probable* cases in Guinea, Liberia, Mali, and Sierra Leone

Data are based on situation reports provided by countries. The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement. Data are missing from Liberia for 4–7 November.

*Data for the past 21 days represent confirmed cases in Guinea, Sierra Leone, and Mali. Data for the past 21 days represent probable cases in Liberia due to the unavailability of systematic district-level data on laboratory confirmed cases before 16 November. Source: World Health Organisation. [2]
Health care workers – HCWs represent at high risk group - total of 639 health-care workers (HCWs) are known to have been infected with EVD (up-to-end of 7 December), 349 of whom have died: in Guinea 121 cases with 62 deaths, Liberia 363 with 174 deaths, Sierra Leone 138 with 106 deaths – for 7 death cases WHO does not precise geographical location. The total case count includes 2 HCWs in Mali, 11 HCWs infected in Nigeria, 1 HCW infected in Spain (while treating an EVD-positive patient), and 3 HCWs in the USA (including a HCW infected in Guinea, and 2 HCWs infected during the care of a patient in Texas) [2].

HISTORICAL OVERVIEW

The first cases of Ebola haemorrhagic fever were described from two outbreaks in two neighbouring locations occurred around the same period: first in Southern Sudan (June-November 1976, with 284 cases including 151 deaths; case fatality was 53%) and subsequently in Northern Zaire, now Democratic Republic of Congo (DRC) – Yambuku province (September – October 1976 with 318 cases including 280 deaths; case fatality 89%). The virus was isolated from patients in both outbreaks named Ebola virus after a small river Ebola in North-western DRC [4, 5].

One year later the virus were identified to be distinct in two species, Zaire ebolavirus (ZEBOV) and Sudan ebolavirus (SUDV) [6]. Over the four decade, Ebola haemorrhagic fever appears sporadically and there have been 23 outbreaks in humans across Africa. According to WHO, from 1976 to 2012 were 2,387 cases reported (including 1,590 deaths) with case fatality 66.6% [1].


INFECTIOUS AGENT

Ebola virus disease is caused by virus from Filoviridae family, genus Ebolavirus, who with other two genera: Marburgvirus and Cucuruvirus complete the family [7]. A total of five Ebolavirus species have been isolated to date. Zaire ebolavirus (ZEBOV), and Sudan ebolavirus (SEBOV) was isolated from the earliest recognised outbreaks of EVD were reported in Zaire and Sudan in 1976. In 1989, Reston ebolavirus, third species of Ebolavirus was isolated from Cynomolgus monkeys imported from the Philippines to a facility in the United States. Serological evidence of infection with this species has been reported in individuals in the Philippines, but no pathogenicity has been reported. Fourth species, Tai Forest ebolavirus was isolated from a veterinarian who had autopsied a chimpanzee in Côte d’Ivoire in 1994, subsequently the virus has not been detected in human. The fifth species Bundibugyo ebolavirus was isolated from patients in the outbreak of EVD in Uganda in 2007 and have been responsible for outbreak in DRC 2012. For almost all previous outbreaks in human reported in Africa was responsible Zaire ebolavirus, who is the most virulent of all Ebolavirus (6). The phylogenetic comparison of the viruses isolated from the patients in the current West Africa outbreak to all 20 genomes from earlier outbreak indicated that the 2014 West African virus instead nesting within the Zaire ebolavirus lineage what suggested initial analysis, most likely diverged from central African lineages around 2004, crossed from Guinea to Sierra Leone in May 2014, and has exhibited sustained human-to-human transmission subsequently, with no evidence of additional zoonotic sources [8]. The Ebola virus samples from this outbreak are 97% similar to the virus that first emerged in 1976. Since discovered Ebola virus has been relatively constant in mutation rate, but have seen no evidence to suggest that ZEBOV may be mutating become more contagious and more easy spread [9].

Ebola viruses are highly infectious agents, biosafety level-4 pathogens, with species Zaire ebolavirus the most virulent of them: require special containment measure and barrier protection. The virus can survive in liquid and dried material for many days. They are inactivated by gamma irradiation, heating for 60 minutes at 60°C or boiling for five minutes, and are sensitive to sodium hypochlorite (bleach) and other disinfectants. Freezing or refrigeration does not inactivate Ebola viruses (10).

RESERVOIR AND MODE OF TRANSMISSION

Reservoir species responsible for maintaining Ebola transmission between outbreaks are not well understood, but researchers now strongly suspect that bats are the natural host for Ebola viruses. The evidence for bats as reservoirs of Ebola viruses comes from numerous epidemiological and ecological studies [11]. During one of the first known Ebola outbreaks, in 1976 in Sudan, the six people who were initially infected worked in a factory room - home to roosting bats. In the large survey of small mammals in and around Gabon, the Central Africa, the three species of bats:
Hypsipetes monstrosus, Epomops franqueti and Myonycteris torquata which were infected with Ebola viruses were identified by the researchers. In a small survey, sampling of 88 fruit bats in surrounding Ghana, West Africa, EBOVs antibodies were detected in serum of five bats species: Epomops franqueti, Epomophorus gambianus, Hypsignathus monstrosus, Nanonycteris veldkampii, and Epomops buettikoferi [12]. This is, as Jonathan Towner, a molecular virologist at the CDC in Atlanta, Georgia in Nature says: “You’re pretty much looking at the entire tropical forest” [13].

Besides known human outbreaks of Ebola virus diseases, there have also been several large epidemics that have had devastating effects on wild primates. In one of them, in 1990s in Côte d’Ivoire, were killed 25% of its members. Because of this high mortality, the scientists have suggested that primates are unlikely reservoir for the virus in the wild [6].

Simon Hay of the University of Oxford and his co-workers from the UK, the USA, and Canada have modeled maps predicting where in Africa wild animals may harbor the virus and where the transmission of the virus from these animals to humans is possible by using the data including: the locations of all recorded primary cases of Ebola in human populations – the “index” cases – many of which have been linked to animal sources; locations of Ebola virus infections in wild bats and primates (chimpanzees, gorillas) from the last forty years, also included new information - collected using satellites—about environmental factors and new predictions of the range of wild fruit bats. Areas in this maps covers 22 countries across Central and West Africa including 22 million people who live in the areas at risk [14].

How people expose to Ebola virus in Africa explain a scientist in the Nature: a team in 2010 reported that as many as 20% of people in some areas of Gabon carry antibodies to Zaire Ebola virus in their blood. This is indicating that they were exposed to the virus in the past without becoming ill [13].

When infected person develop symptoms, human-to-human transmission can occurs through:

- direct contact with the blood or body fluids (including but not limited: faeces, saliva, sweat, urine, vomit and semen), organs from person who is infected, (in the current outbreak each person with Ebola will infect 1-2 person, therefore is less contagious then many common diseases such as mumps and measles, where one person with Ebola will infect 5-7 person, respectively 12-18 person [7, 15];
- contacts with objects (e.g. needles, syringes, linen, clothes) contaminated with blood or body fluids of infected persons or animals. In the African’s countries where burial ceremonies in which mourners have direct contact with the body of the deceased person, also plays a role in the transmission of Ebola [7].

People remain infectious (period of communicability) as long as their blood and body fluids, including semen and breast milk, contain the virus. According to WHO evidence, seminal fluids of convalescing men can shed the Ebola virus for at least 82 days after onset of symptoms. Although the scientific evidence is limited, it is clear that semen is a potential source of infection and could therefore cause transmission of the virus through delivery of the infectious virus on a mucosal surface [16].

The virus in blood and fluids can enter to another person through damaged skin and unprotected mucosa, or example eyes, nose and mouth [1].

**Symptoms of Ebola virus disease**

The time interval from infection with the virus to onset of symptoms - the incubation period of EVD – ranges from 2 to 21 days, in average 8-10 days. The first symptoms in most of infected patients are: sudden onset of flu-like illness with fever >38.6 °C, malaise (weakness), muscle and joint pains and headache, followed by progressive weakness, anorexia, diarrhea (watery stools sometimes containing blood and mucus), nausea and vomiting, what to corresponds to the prodromal phase (duration up to 10 days).

The next stage of the disease is characterized by symptoms and clinical manifestations from several organ systems: gastrointestinal (vomiting, diarrhea, anorexia and abdominal pain), neurological (headaches, confusion), vascular (conjunctive/pharyngeal injections), cutaneous (maculopapular rash), and respiratory (cough, chest pain, shortness of breath), and can include complete exhaustion (prostration). Hemorrhagic manifestations (bloody diarrhea, nosebleeds, hematemesis, petechiae, ecchymosis and prolonged bleeding from needle puncture sites) can appear in more than half of the patients after one week of evolution, with develop in some patients’ internal and external hemorrhages and disseminated intravascular coagulation. In the final stage patients die with clinical signs of tachypnea, anuria, hypovolemic shock and multiorgan failure. Depending on the viral species, as previously stated based on previous outbreaks, 25% to 90% of cases may die. Recovered patients will develop immunity lasting at least 10 years [17].

Results of the study based on data collected during surveillance and response activities of WHO Ebola Response team for EVD in Guinea, Liberia, Nigeria and Sierra Leone in the first 9 months in the current epidemic in West Africa 2014, shows that the most common symptoms onset and case detection include: fever (81.7%), fatigue (76.4%), loss of appetite (64.5%), vomiting (67.6%), diarrhea (65.6%), head-
ache (53.4%), and abdominal pain (44.3%). Specific haemorrhagic symptoms were rarely reported (in <1% to 5.7% of patients). “Unexplained bleeding” was reported in 18.0% of cases. The measure of the period of infectiousness in the community, the mean time plus/minus (±) 1 standard deviation, from the onset of symptoms to hospitalization, was 5.0±4.7 days. The mean time to death after admission to the hospital was 4.2±6.4 days, and the mean time to discharge was 11.8±6.1 days. These patterns are similar in each country. Based on this WHO Ebola Response team concluded that the clinical courses of infection according to clinical characteristics of patients in the previous EVD outbreaks are similar [3].

**Diagnosis**

Early diagnosis of Ebola virus disease is difficult, because the early symptoms, such as fever, fatigue, muscle aches and joint pain, headaches are nonspecific and may be seen in patients with more frequent diseases in Africa (malaria, typhoid fever). Because of this, Ebola patients initially may go undiagnosed. However, people who have some of the symptoms typical for Ebola, and if there is information that has been in contact with the infected person with Ebola, or with contaminated objects with blood or body fluids of people with Ebola, or has been in contact with an infected animal all these fit to the epidemiological linkage, the patient should be isolated and public health care institutions should be reported. The three leading institutions: Centre for Control and Prevention Diseases (CDC), Atlanta, World Health Organisation (WHO) and European Centre for Control and Prevention Diseases (ECDC) developed “Algorithm for initial assessment and management of patients for EVD”, as well as “Algorithm for laboratory diagnosis of EVD” [18, 19].

Diagnosis of EVD is made most commonly through detection of Ebola virus RNA or Ebola virus antibodies in blood. In the current outbreak in West Africa, testing patients’ specimen for Ebola virus performed: by Institute Pasteur, the European Mobile Laboratory, and CDC in Guinea; by the Kenema Government Hospital Viral Hemorrhagic Fever Laboratory in Sierra Leone; and by the Liberia Institute of Biomedical Research [20].

**Treatment**

There is currently no specific treatment - vaccine or medications (such as antiviral drugs) that have been proven to be effective in treating Ebola. The scientific community has proposed numerous experimental interventions, including: vaccines, convalescent blood and plasma antiviral medicines and other medicines, but none of these interventions have been evaluated for efficacy against EVD. They required clinical study to assess their safety and efficacy. The clinical trials should only be conducted in facilities able to provide consistently good standard of care, concluded the experts of EBV on the meeting of the Scientific and Technical Advisory Committee for Ebola Experimental Interventions (STAC-EE) in Geneva, on 11-12 November 2014 [21].

The World Health Organization (WHO) convened an urgent meeting on 29 and 30 September 2014 to assess the efforts under way to evaluate and produce safe and effective Ebola vaccines as soon as possible. Two vaccine candidates currently being tested in humans: the chimpanzee adenovirus serotype 3-cAd3-ZEBOV vaccine, and the recombinant vesicular stomatitis virus-rVSV-ZEBOV vaccine. Both vaccine candidates have demonstrated 100% efficacy in studies in non-human primates, but how that will translate to human subject’s remains unknown [22]. Phase I clinical trials on healthy adults in countries with no (or very few) Ebola will use dose-response designs structure to determine the level of humoral and cellular immunity that can be induced. Because of the small numbers of participants in these trials, they will provide data only on common adverse events and the minimum antibody titre needed to confer protection in humans is unknown [22]. If the results in phase 1 are favourable, the phase II trials to take place in several countries with no or few cases of EVD in West Africa in January 2015 and this trial will test safety and capacity to induce an immune response in larger numbers and in broader populations, including the elderly, children, and persons living with HIV [21, 22].

Early treatment of Ebola symptoms, as they appear, can significantly improve to chance survival that including: supportive therapy, rehydration with a balanced electrolyte (intravenous or oral fluids), maintaining the status of oxygen and blood pressure and treating other infection if they occur [1].

**Prevention and control**

The three leading institutions CDC Atlanta, WHO and ECDC, with respect to modes of transmission of Ebola virus, agrees that good outbreak control relies on applying a package of interventions, namely case management, which include: early diagnosis, patients isolation, contact tracing, a good laboratory services, safe burials and social mobilisation. Risk reduction should focus on [1, 17, 20]:

- **Reducing the risk of wildlife-to-human transmission** in such a way animals should be handled with gloves and other appropriate protective clothing;
animal products (blood and meat) should be thoroughly cooked before consumption [1].

- **Reducing the risk of human-to-human transmission** from direct or close contact with people with Ebola symptoms, particularly with their bodily fluid, also should be worn appropriate personal protective equipment, hand washing, when taking care ill patients at home or visiting in hospital [1]. **WHO insists on avoiding any home treatment** [1].

  - **Outbreak containment measures** including: prompt and safe burials ceremony, identifying people who may have been in contact with someone infected with Ebola, monitoring the health of contacts for 21 days, separating the healthy from the sick, good hygiene and maintaining a clean environment [1].

Health-care workers should apply extra infection control measures with caring for patients with suspected or confirmed Ebola virus to prevent contact with the patient’s blood and body fluids and contaminated surfaces or materials such as clothing and bedding. When in close contact (within 1 meter of patients with EBV), health-care workers should wear face protection (a face shield or a medical mask and goggles), a clean, non-sterile long-sleeved gown (no one part of detected body), and gloves (sterile gloves for some procedures) [1].

For efficient prevention and control measures, it is important to underline that the virus is inactivated by gamma irradiation, heating for 60 minutes at 60°C or boiling for five minutes, and are sensitive to sodium hypochlorite (bleach) and other standard disinfectants. Freezing or refrigeration does not inactivate Ebola viruses [10].

The CDC, Atlanta and WHO have developed a set of guidelines to assist in the prevention and spread of Ebola, entitled “Infection Control for Viral Haemorrhagic Fevers in the African Health Care Setting”. The guide describes how to identify a case of viral hemorrhagic fever and how to prevent transmission of infections within healthcare institutions using local available materials and with minimal financial resources. Further, developed guides or interim guidelines for infection control Ebola virus in hospitals, guidelines for collecting the samples, transportation and testing of people suspected of infection by Ebola virus, guidelines for air transport / quarantine, etc. [23, 24].

According to the WHO guidance for countries with no reported cases of Ebola virus diseases, entitled “Ebola surveillance in countries with no reported cases of Ebola virus disease” which describes what should be taken by the competent authorities of the country, include: an alert system which should be in place at the major land border crossing with already affected countries, capital cities, including airports, seaports, and health care facilities, especially in major hospitals. The staff of alert system should be trained in case definition and able to detect signs and symptoms of disease, and should report sick persons coming from country that has reported cases of Ebola virus diseases, infection prevention and control measures. Alert system also include isolation centre and dedicated staff trained in infection prevention and control measures, identification national or international WHO recognised reference laboratory [25].

In our country the organizations of health institutions are taking all prevention measures in accordance with WHO recommendations [26].

**Declaration of interest**

The authors declare no conflict of interest for this study.

**References**


ENISA ADEMOVIĆ, SEMRA ČAVALJUGA: EBOLA VIRUS DISEASE – AN OVERVIEW OF THE 2014 OUTBREAK IN WEST AFRICA


