Global Veterinaria 15 (5): 532-535, 2015
ISSN 1992-6197

DOI: 10.5829/idosi.gv.2015.15.05.101177

Overview of Ebola Virus in Africa

Kawther S. Zaher

Department of Microbiology and Immunology, National Research Centre, Dokki, Egypt, 60014618

Abstract: Ebola virus is a negative sense non segmented RNA virus belongs to Filoviridae family. There are five sub-types of Ebola virus Zaire Ebolavirus (ZEBOV), Reston Ebolavirus (RESTV), Sudan Ebolavirus (SUDV), Taï Forest Ebolavirus (TAFV) and Bundibugyo Ebolavirus (BDBV). Zaire Ebolavirus and Sudan Ebolavirus are the most lethal subtypes with high infectiousness and pathogenicity. The virus is cylindrical in shape, enveloped and it has seven structural proteins: nucleoprotein (NP), polymerase cofactor (VP35), membrane-associated proteins: matrix (VP40), glycoprotein GP, transcription activator minor nucleoprotein (VP30), minor matrix VP24 and RNA-dependent RNA polymerase (L). The main mode of transmission is by fruit bat and with direct contact with sick people or contaminated fluid or vessels with the virus. Early symptoms of Ebola virus disease include flu-like illness while the next stage of the disease can be gastrointestinal, neurological, cutaneous and respiratory. During the first week, patients often deteriorate suddenly, while diarrhea and vomiting are getting worse. After one week, hemorrhagic manifestations can appear in more than half of the patients and some patients develop profuse internal and external hemorrhages and disseminated intravascular coagulation. Patients in the final stage of disease die in the clinical picture of massive bleeding, metabolic disturbances, severe dehydration, hypovolemic shock and multi-organ failure. The most preferred diagnostic test is RT-PCR of the blood followed by Antigen-capture ELISA which is less sensitive than RT-PCR. Other tests such as rapid immune-chromatographic assay and rapid recombinase polymerase amplification (RPA) are used for diagnosis of the virus. Analysis of sequenced EBOV whole genome revealed that the Guinean strain and the Central African strains belonged to different clusters and the viruses currently circulating in Sierra Leone has diverged from Central African strains. Also researches have attributed this diversion to fruit bats. Vaccines, antibodies, siRNAs (small interfering RNAs), interferons and chemical substances, biological substance (The cyanobacterial lectin scytovirin (SVN)) and a variety of compounds that have been found to inhibit EBOV infection by blocking viral entry or by a mode of action that still has to be resolved. Unfortunately, all of them are in trial phase and not expected to be for commercial use yet.

Key words: Ebola virus · EBOV · Ebola virus disease · Risk Group 4 Pathogen

INTRODUCTION

Ebola is an envelope, non-segmented, negative-sense RNA-virus that belongs to the family Filoviridae [1]. Ebola virus (EBOV) was discovered in 1976 in a village near Ebola River, from which the disease takes its name. The Ebola epidemic occurs primarily in central and western Africa and Philippines [2]. Five Ebola virus sub-types have been discovered, which are Zaire Ebolavirus (ZEBOV), Reston Ebolavirus (RESTV), Sudan Ebolavirus (SUDV), Taï Forest Ebolavirus (TAFV) and Bundibugyo Ebolavirus (BDBV). Zaire Ebolavirus and Sudan Ebolavirus are the most lethal subtypes with high infectiousness and pathogenicity. Unfortunately, no effective treatments and licensed vaccines are available for EBOV infection [3, 4].

Virus Molecular Structure: The EBOV genome is a single-stranded RNA approximately 19,000 nucleotides long. It encodes seven genes, which encode for seven structural proteins: nucleoprotein (NP), polymerase cofactor (VP35), membrane-associated proteins: matrix (VP40), glycoprotein GP, transcription activator minor nucleoprotein (VP30), minor matrix VP24 and RNA-dependent RNA polymerase (L) [5].

Corresponding author: Kawther S. Zaher, Department of Microbiology and Immunology, Veterinary Research Division, National Research Centre, Dokki, Giza, Egypt. Postal cod: 12622. E-mail: zaherkus@yahoo.com.

EBOV is cylindrical/ tubular and contain viral envelope, matrix and nucleocapsid components. The overall cylinders are generally approximately 80 nm in diameter and have a virally encoded glycoprotein (GP) projecting as 7-10 nm long spikes from its lipid bilayer surface. The cylinders are of variable length, typically 800 nm, but sometimes up to 1000 nm long [6].

Mode of Transmission, Entry and Replication: EBOV is a zoonotic pathogen. Intermediary hosts have been reported to be various species of fruit bats, throughout central and sub-Saharan Africa. Evidence of infection in bats has been detected through molecular and serologic means. However, EBOV have not been isolated in bats. End hosts are humans and great apes, infected through bat contact or through other end hosts. Pigs on the Philippine islands have been reported to be infected with the virus, so amplifying hosts may exist [7]. The virus spreads by direct contact with body fluids, such as blood of infected human or other animals. This may also occur through contact with an item recently contaminated with bodily fluids. Spread of the disease through the air between primates, including humans, has not been documented in either laboratory or natural conditions. Semen or breast milk of a person after recovery from Ebola virus disease (EVD) may still carry the virus for several weeks to months [8].

There are two candidates for host cell entry proteins. The first is a cholesterol transporter protein, the host-encoded Niemann-Pick C1 (NPC1), which appears to be essential for entry of Ebola virions into the host cell and for its ultimate replication. The second candidate is TIM-1 (aka HAVCR1). TIM-1 was shown to bind to the receptor binding domain of the EBOV glycoprotein, to increase the receptivity of Vero cells [9-11].

From the above motioned data, these studies suggest NPC1 and TIM-1 may be potential therapeutic targets for an Ebola anti-viral drug and as a basis for a rapid field diagnostic assay.

Clinical Signs: EBOV is one of the highest case-fatality rates among virus diseases, averaging 83 percent since the first outbreaks in 1976, although fatality rates up to 90 percent have been recorded in one outbreak (2002–03). The first outbreak occurred on 26 August 1976 and the symptoms resembled malaria and subsequent patients received quinine. Transmission has been attributed to reuse of unsterilized needles and close personal contact, body fluids and places where the person has touched.

The onset of EVD is sudden and early symptoms include flu-like illness accompanied by fever, fatigue, headache and sore throat. The next stage of the disease can be gastrointestinal (vomiting, diarrhea, anorexia and abdominal pain), neurological (headaches, confusion), cutaneous (maculopapular rash) and respiratory (cough, chest pain, shortness of breath) and can include complete exhaustion (prostration). During the first week, patients often deteriorate suddenly, while diarrhea and vomiting are getting worse. All of these symptoms correspond to the prodromal phase of EVD. After one week, hemorrhagic manifestations can appear in more than half of the patients (bloody diarrhea, nosebleeds, hematemesis, petechiae, ecchymosis and puncture bleedings). Some patients develop profuse internal and external hemorrhages and disseminated intravascular coagulation. Patients in the final stage of disease die in the clinical picture of massive bleeding, metabolic disturbances, severe dehydration, diffuse coagulopathy, tachypnea, anuria, hypovolemic shock and multi-organ failure [12].

Diagnosis: The most preferred diagnostic test is RT-PCR of the blood. RT-PCR targeting the NP can be performed in the serum, whole blood, plasma, or oral fluid. Antigen-capture ELISA can also be used on blood samples, but is less sensitive than RT-PCR [13]. A rapid immunochromatographic assay for the detection of EBOV antigen, which claimed to provide result in 15 min, was recently announced by the France's Atomic Energy Commission [14]. Most recently rapid recombinase polymerase amplification (RPA) EBOV detection assay is established and it yielded a sensitivity and specificity of 100% in reference to one real-time RT-PCR assay [15].

Phylogentic analysis of EBOV by the whole genome sequencing of the virus has revealed that the Guinean strain and the Central African strains belonged to different clusters. A more recent description of the viruses currently circulating in Sierra Leone, indicated that the virus has diverged from Central African strains since 2004 [16, 17]. The circulation of EBOV in the West African tropical forest can be accounted for the distribution area of the fruit bat species which act as a reservoir host and covers the whole African tropical forest, from Tanzania to Casamance (Senegal) and to further countries in west and central Africa. The transmission of the virus between fruit bat and human is not rare due to bat consumption of fruit [18]. Fig 1 shows Phylogenetic analysis of EBOV species and of EBOV strains from Equatorial and West Africa. The phylogenetic trees are based on the first 6000 nucleotides of the viral genome, including nucleoprotein, VP35 and VP40 coding sequences.

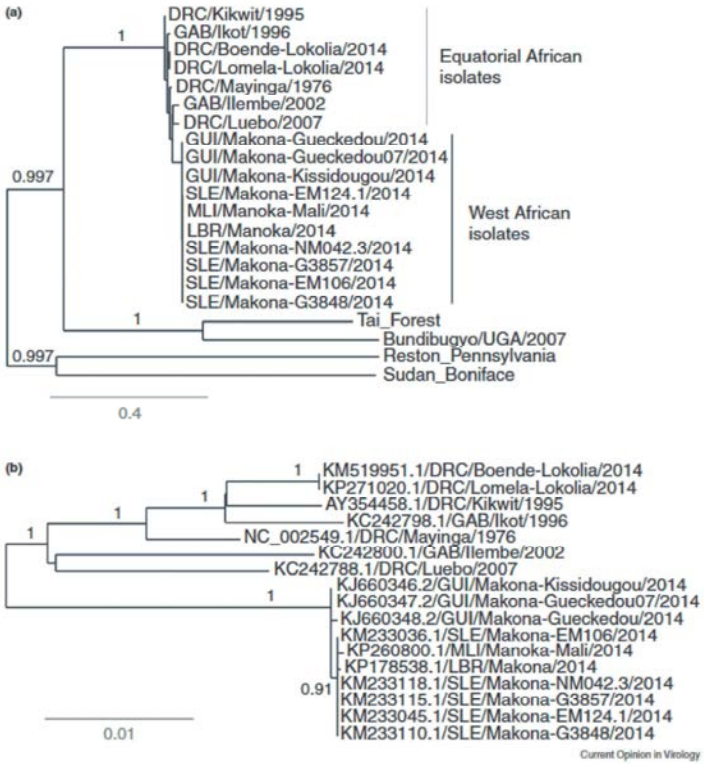

Fig 1: Phylogenetic analysis of Ebolavirus species and of Ebola virus strains from Equatorial and West Africa. (a) Phylogenetic analysis of the different Ebolavirus species. For clarity purpose, Taı¨ Forest, Bundibugyo, Sudan and Reston viruses are represented by a single prototypic sequence. A representative panel of different Zaire Ebolavirus sequences has been analyzed, from viruses isolated in DRC, Gabon (GAB), Guinea (GUI), Sierra Leone (SLE), Mali (MLI) and Liberia (LBR). (b) Phylogenetic analysis of the different Zaire Ebolavirus isolates clearly showing that Equatorial and West African isolates formed distinct clusters. The same sequences as in (a) have been analyzed. The GenBank accession numbers of sequences are noted. The phylogenetic trees are based on the first 6000 nucleotides of the viral genome, including nucleoprotein, VP35 and VP40 coding sequences [18].

Therapeutic Strategies Against EBOV: vaccines, antibodies, siRNAs (small interfering RNAs), interferons and chemical substances, i.e. neplanocin A derivatives (i.e. 3- deazaneplanocin A), BCX4430, favipiravir (T-705), endoplasmic reticulum (ER) a-glucosidase inhibitors, biological substance (The cyanobacterial lectin scytovirin (SVN)) and a variety of compounds that have been found to inhibit EBOV infection blocking viral entry or by a mode of action that still has to be resolved. Vaccines involve recombinant and subunit vaccines which are all in trial phase and not expected to be for commercial use yet [19]. Cyanobacterial lectin scytovirin (SVN) which has the ability to binds with high affinity to mannose-rich oligosaccharides on the envelope glycoprotein (GP) of a number of viruses, blocking entry into target cells, has managed to bind to the envelope GP of Zaire Ebola virus (ZEBOV) and inhibit its replication [20]. Unfortunately, the majority of other compounds are targeted at either viral entry or virus replication/transcription.

REFERENCES

1. Feldmann, H. and T. Geisbert, 2011. Ebola haemorrhagic fever. Lancet, 277(9768): 849-862.
2. Peterson, A.T., J.T. Bauer and J.N. Mills, 2004. Ecologic and geographic distribution offilovirus disease. Emerg. Infect. Dis., 10(1): 40-47.
3. Kuhn, J.H., S. Becker, H. Ebihara, T.W. Geisbert, K.M. Johnson, Y. Kawaoka, W.L. Lipkin, A.I. Negredo, S.V. Netesov, S.T. Nicjol, G. Palacios, C.L. Peters, A.E. Volchkov and P.B. Jahrling, 2010. Proposal for a revised taxonomy of the family filoviridae: classification, names of taxa and viruses and virus abbreviations. Arch. Virol., 155(12): 2083-2103.

4. Kuhn, J.H., S. Becker, H. Ebihara and T.W. Geisbert, 2011. Family Filoviridae. In: A.M.Q. King, M.J. Adams, E.B. Carstens and E.J. Lefkowitz (Eds.), Virus Taxon-omy: Ninth Report of the International Committee on Taxonomy of Viruses. Elsevier/Academic Press, London, UK.
5. Stahelin, R.V., 2014. Membrane binding and bending in Ebola VP40 assembly andegress. Front. Microbiol., 5: 300.
6. Klenk, H.D. and H. Feldmann, 2004. Ebola and Marburg Viruses – Molecular and Cellular Biology. Wymondham, Norfolk, UK: Horizon Bioscience. ISBN 978-0-9545232-3-7.
7. Feldmann, H., 2014. "Ebola-A Growing Threat?". N. Engl. J. Med., 371(15): 1375-8.
8. WHO, 2014. "2014 Ebola Virus Disease (EVD) outbreak in West Africa". WHO. 21 April 2014. Retrieved 3 August2014.
9. Carette, J.E., M. Raaben, A.C. Wong, A.S. Herbert, G. Obernosterer, N. Mulherkar, A.I. Kuehne, P.J. Kranzusch, A.M. Griffin, G. Ruthel, P. Dal Cin, J.M. Dye, S.P. Whelan, K. Chandran, T.R. Brummelkamp, R. Wong, H. Obernosterer, M. Kuehne, K. Griffin, R. Dal Cin, D. Whelan and C. Brummelkamp, 2011. Ebola virus entry requires the cholesterol transporter Niemann-Pick C1. Nature, 477(7364): 340-3.
10. Côté, M., J. Misasi, T. Ren, A. Bruchez, K. Lee, C.M. Filone, L. Hensley, Q. Li, D. Ory, K. Chandran, J. Cunningham, M. Ren, B. Lee, F. Hensley, L. Ory and C. Cunningham, 2011. Small molecule inhibitors reveal Niemann-Pick C1 is essential for Ebola virus infection. Nature, 477(7364): 344-8.
11. Flemming, A., 2011. Achilles heel of Ebola viral entry. Nat. Rev. Drug Discov., 10(10): 731.
12. Roddy, P., N. Howard, M.D. Van Kerkhove, J. Lutwama, J. Wamala and Z. Yoti, 2012. Clinical manifestations and case management of Ebola haemorrhagic fever caused by a newly identified virus strain, Bundibugyo, Uganda, 2007-2008. PLoS One, 7: 52986.
13. Formenty, P., E.M. Leroy, A. Epelboin, F. Libama, M. Lenzi and H. Sudeck, 2006. Detection of Ebola virus in oral fluid specimens during outbreaks of Ebola virus hemorrhagic fever in the Republic of Congo. Clin Infect Dis., 42: 1521e6.
14. Kelvin, K.W., J.F.W. Chan, A.K.L. Tsang, V.C.C. Cheng and K.Y. Yuen, 2015. Ebola virus disease: a highly fatal infectious disease reemerging in West Africa. Microbes and Infection, 17(20): 84e97.
15. Faye, O., O. Faye, Bé. Soropogui, P. Patel, A.A. El Wahed, C. Loucoubar, G. Fall, D. Kiory, N.F. Magassouba, S. Keita, M.K. Kondé, A.A. Diallo, L. Koivogui, H. Karlberg, A. Mirazimi, O. Nentwich, O. Piepenburg, M. Niedrig, M. Weidmann and A.A. Sall, 2015. Development and deployment of a rapid recombinase polymerase amplification ebola virus detection assay in guinea in 2015. Eurosurveillance, 20(44): pii-30053.
16. Baize, S., D. Pannetier, L. Oestereich, T. Rieger, L. Koivogui, N.F. Magassouba, B. Soropogui, M.S. Sow, S. Keita and H. De Clerck, 2014. Emergence of Zaire Ebola virus disease in Guinea. N Engl J Med., 371: 1418-1425.
17. Gire, S.K., A. Goba, K.G. Andersen, R.S.G. Sealfon, D.J. Park, L. Kanneh, S. Jalloh, M. Momoh, M. Fullah and G. Dudas, 2014. Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak. Science, 345: 1369-1372.
18. Baize, S., 2015. Ebola virus in West Africa: new conquered territories and new risks or how I learned to stop worrying and (not) love Ebola virus. Current Opinion in Virology, 10: 70-76.
19. De Clercq, E., 2015. Ebola virus (EBOV) infection: Therapeutic strategies. Biochemical Pharmacology, 93(4): 1-10.
20. Garrison, A.R., B.G. Giomarelli, C.M. Lear-Rooney, C.J. Saucedo, S. Yellayi, L.R.H. Krumpe, M. Rose, J. Paragas, M. Bray, G.G. Olinger, J.B. McMahon, J. Huggins and B.R. O'Keefe, 2014. The cyanobacterial lectin scytovirin displays potent *in vitro* and *in vivo* activity against Zaire Ebola virus Antiviral Research, 112(6): 1-7.