Journal of Pharmacy Practice and Community Medicine.2016, 2(2): 35-39 • http://dx.doi.org/10.5530.jppcm.2016.2.3 e-ISSN: 2455-3255

REVIEW ARTICLE

OPEN ACCESS

Past, Present and Future about Ebola Virus Diseases: An Updated Review

Akash Mali*[1], Bodake Swapnil[2], Jadhav Pooja[3], Mali Dwaraka[4], Jurgelevičius Vaclovas[5]

[1]*Department of Molecular Biology and Biotechnology, University of Wurzburg, Wurzburg, GERMANY.*

[2]*Department of Nursing, ANM, Government Hospital, ZP, Satara, Maharashtra, INDIA.*

[3]*Department of Pharmacy, HelpageIndia, Organization, Khandala, Maharashtra ,INDIA.*

[4]*Department of Pharmacology, SDVV College of Pharmacy and Research Center Panvel, Mumbai, INDIA.*

[5]*Department of Laboratory Diagnostics, Senior Scientist, Vytautas Magnus University, Lithuania, EUROPE.*

Received: 02 January 2016 ;

Accepted: 09 February 2016

***Correspondence to:**

Mr. Akash Mali,

Department of Molecular Biology and Biotechnology, University Of Wurzburg, Wurzburg, GERMANY.

E-mail: Akashmit97@gmail.com

Copyright: © the author(s),publisher and licensee Indian Academy of Pharmacists. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Ebola virus is responsible for the Ebola virus diseases. The epidemic of Ebola hemorrhagic fever is a deadly disease of animal can also be transmitted to human and non-human primates. The virulence of Ebola virus involved in several immune evasion mechanisms that include an inhibition of type I interferon responsible for innate immunity, epitope masking, etc. recently Ebola virus is sexually transmitted which was reported in Liberia has associated with new clusters in regions previously declared Ebola-free. There is no appropriate antiviral vaccine or therapy is not available to work against EBOV infection in humans. However, supportive recovery practices are performed include high-fluid intake, ventilator support and broad-spectrum antibiotic therapy. The treatment and diagnosis is very important because these kind of dangerous viruses are possibly used for bio-weapons. The present review describes briefly about virology, epidemiology, pathophysiology, transmission, diagnosis and treatment of Ebola viral disease.

Key words: Ebola virus, Filovirus, RT-PCR, Drug,Vaccine Development.

INTRODUCTION

Ebola virus is Precarious corresponding to Ebola virus disease (EVD). Ebola first appeared in 1976 in two simultaneous outbreaks, in Nzara, Sudan, and in Yambuku, Democratic Republic of Congo.[1,2] It has not been reported in humans in the Asia Pacific region as of 31 July 2012. However, with global traveling it is possible that outbreaks in Africa could result in the spread of the virus to Asia specifically in India. There are different species of the Ebola virus. Of these, the Reston ebola virus was first discovered in laboratories in Reston, Virginia, United States of America (USA) in 1989 after some quarantined, crab-eating macaque monkeys originating from the Philippines became ill and died. In 2008, a virus identified in pigs was found to be very similar to the virus identified in monkeys imported into the USA for research from the Philippines in 1989.[3] The World Health Organization has declared a public health emergency of international concern and also called all nations for a coordinated international response to investigate, detect and manage Ebola cases.[4]

Virology

Filoviruses (family Filoviridae) are enveloped, linear, Class V, (-) SS-RNA viruses belonging to the order Mononegavirales. Ebolavirus and Marburgvirus are the two genera of filoviruses that have been identified to cause severe disease in humans.[5,6] Five Ebola virus species (Bundibugyo ebolavirus, Zaire ebolavirus, Sudan ebolavirus, Reston ebolavirus, Taï Forest (formerly Côte d'Ivoire ebolavirus) First four cause Ebola virus disease in humans and a fifth species has only caused disease in nonhuman primates. Virions of the EBOV genome are made with a core of single negative-sensed RNA, also contain proteins such as viral proteins 24, 30, 35 and 40, nucleoprotein,

Publishing Partner : EManuscript [www.emanuscript.in]

L protein and glycoprotein (GP). The structural similarity of genome among the species brings a wide genetic divergence. In addition, phylogenetic analysis of GP gene sequences of EBOV confirmed that epidemic EBOV-Z strains shown close genetic relationships.[7]

Ebola Outbreaks

According to Ebola Situation Report In West African Countries more than 11,000 deaths and 28500 Suspected Cases are found, Recently there is no conform victim found From Dec 2015 to 6 Jan 2016, due to migration It is spread in European countries, suspected cases found in Spain, Italy and United kingdom, the worldwide Suspected cases shown in Figure 2 (WHO 2016).

Epidemiology

The filovirus hemorrhagic fever was primarily recognized in Germany and Yugoslavia in 1967. The causative virus was named as Marburg virus.[9] Southern Sudan and Northern Zaire were affected with an epidemic of hemorrhagic fever was reported in 1976. In the name of Ebola River, located in the north western Democratic Republic of the Congo, an uncertain infectious agent was named as the Ebola virus. In 1994, the third Ebola virus species were found in the Tai forest where an ethnologist had performed the post-mortem examination on chimpanzee was living with other members of its species were dying due to EHF.[10] The Ebola virus had primarily identified in the area of the rain forests of Central Africa. In recent, it entered epidemically to the distant villages of Central and Western Africa. WHO, CDC (Center for Disease Control), and many international associations have updated the recent knowledge about EVD to students, travelers and clinicians. The high fatality rate (60-90%) of EVD outbreaks depends on the accessibility of appropriate medication, time of diagnosis, and EVD subtype (WHO, 2015).

Pathogenesis and transmission

The transmission of Ebola virus is due to close reside with the wild animals like chimpanzees, baboons, African green monkeys, duikers and fruit bats (*Myonycteris torquata* and *Pteropodidae, Hypsignathus monstrosus, Epomops franqueti.)*.[11] The possibility of sexual transmission owing to the presence of EBOV RNA in semen and vaginal secretions[12] Plants, birds and arthropods were become as possible reservoirs of ebola virus. EVD outbreaks (2001 and 2003) with traces of ZEBOV were found in the carcasses of chimpanzees and gorillas are the source of human infections. The first Ebola outbreak in Congo was due to re-usage of unsterilized needles and syringes were a crucial factor in the transmission of Ebola virus. The Kikwit outbreak of Ebola virus was because of improper protective measures of several clinicians.[13] The fatality of EHF was due to the evidence of the increase of interferon-alpha and gamma, interleukin 2 and 10 and tumor necrosis factor in blood. More noticeable effects caused by Ebola virus include changes in vascular permeability, micro vascular damage and activation of the clotting cascade and also involve in impairment of endothelial cells and platelets cause imbalance of homeostasis. The persistence of virus in semen up to 7 weeks it indicates that the probability of ebola transmission in sexual mode. The spread of EBOV infection to infants through breast milk, making the kid infected.[14] Transmission does not occur during the incubation period and only occurs once an infected person present with symptoms. In Burial ceremonies mourners have direct contact with the body of the diseased person can also play a vital role in the transmission of Ebola. And there is possibility to transmit the virus through semen by men who was recovered from disease up to 3 months.[15] ZEBOV has the most severe mortality rate of 90%, where as Sudan ZEBOV (SEBOV) have shown 53-66% mortality rate[16] An incubation period of EVD is 2-21 days (Avg. 4-10 days). Severely infected patients die within 6-9 weeks after the first symptoms appear. In most outbreaks, slow disease identification leads to increasing the death rates due to unfamiliar and non-specific symptoms of new illness are difficult for physicians to identify at initial stage.

Diagnosis

Since the Ebola virus has been classified by the CDC as a pathogen of category A, the category that includes most dangerous pathogens causing diseases with high morbidity and mortality, viral diagnosis should be performed only in specialized laboratories with the highest level of biosafety, i.e. BSL-4. It should be fast, sensitive and specific, and the methodology used should greatly limit the possibility of exposure of a person engaged in the study to the risk of the laboratory infection. The selection of the tests is also dependent on the capabilities of performers being under different conditions, even at the site of the epidemic outbreaks. Currently, real time RT-PCR is considered as the most sensitive method, which allows for detection of the number of viral copies in specimen. Although there are other methods of virus identification. But the presence of viral RNA can be detected by polymerase chain reaction with reverse transcription (RT-PCR) even after 48 h post onset. However, it should be emphasized that due to continuous virus mutations RT-PCR method may be unreliable and results should be confirmed by other assay.

Table 1: Drug Development For EVD

Drugs	Mechanism of Action	Animal models	Clinical Trials
Monoclonal Antibody(ZMapp) By Nicotiana benthamiana	13C6 binds at the tip of the viral glycoprotein, perpendicular to the plane of the viral membrane	Human and human mouse chimeric mAbs(cl3C6, h13F6, and c6D8) ZMab mouse(m1H3, m2G4, and m4G7)	Phase II
TKM-Ebola	Combination of small interfering RNAs that target Ebolavirus RNA polymerase L,formulated with lipid nanoparticle technology	non-human primates, guinea pigs, monkeys	Phase II
Brincidofovir (CMX-001)	*In vitro*-treatment of cytomegalovirus and adenovirus	Humans	Undergoing Phase III
AVI-7537	Antisense phosphorodiamidate morpholinooligomers(PMOs)that target the Ebolavirus VP24gene	non-human primates	Phase I
BCX-4430	Inhibition of viral RNA dependent RNA polymerase	non-human primates and rodents	Phase I
Interferons, amiodarone, clomiphene, and chloroquine, amiodarone	Inhibit Ebola virus interactions with human cells in models	Humans	Phase III

Table 2: Vaccine Development

Vaccines	Properties	Clinical Trials
cAd3 Ebola Vaccine(Chimp Adenovirus type 3)+GP	Trials in NHPs elicited Immunogenic Response against lethal Challenge	Phase I
Recombinant DNA Vaccine(rVSV,rRABV,rHPIV3,rCMV	Trials on Non-Human Primates elicited Immunogenic Response against lethal Challenge, Highly Species Specific	Phase I

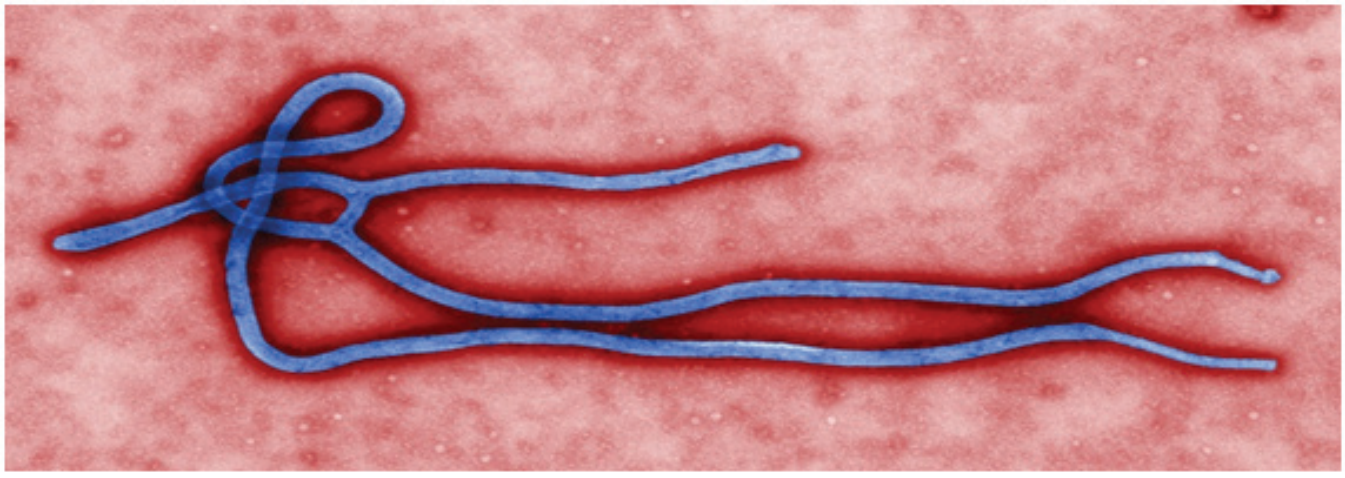


Figure 1: Transmission Electron Micrograph (TEM) of Ebola Virus Virion

One-tube real-time RT-PCR assay was developed for identification of ZEBOV and SEBOV.(20) To distinguish between Ebola virus species and strains sequencing of amplified genomic RNA can also be used.[17] The enzyme-linked immunosorbent assay (ELISA) may be used to detect both antibodies as well as virus-specific antigens. Assays for the detection of antibodies are less useful because the patient often dies before the formation of specific antibodies. Therefore, they are carried out mainly for epidemiological purpose, for patients who survived this terrible disease. Positive results obtained by the ELISA can be confirmed by Western blot. Sometimes only IgM antibodies are detectable in specimen of sick person.[18] Currently applied assays use monoclonal antibodies against different viral proteins, e.g. VP40. Virus isolation in cell cultures is one of the very sensitive methods. Acute phase patient sera or

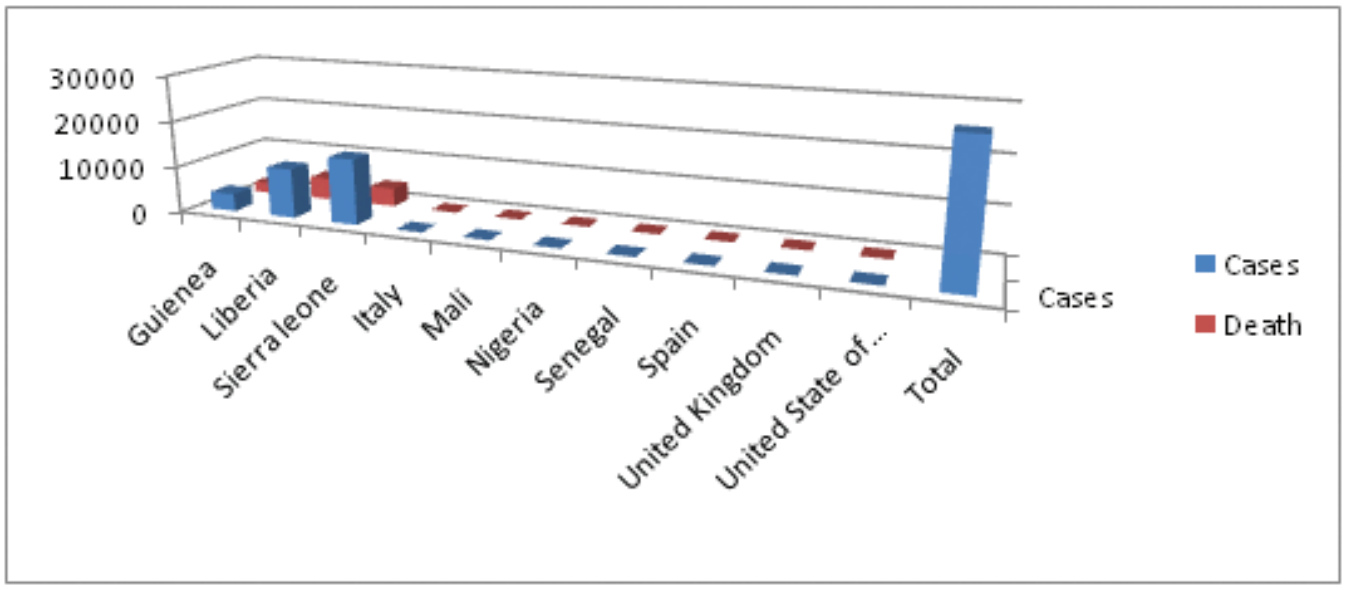


Figure 2: Worldwide suspected EVD cases Up to 6 Jan 2016 by WHO 2016

postmortem tissue samples may be appropriate material for the virus isolation. Ebola virus is able to replicate in numerous cell lines and virus growth can be detected by cytopathic effect. Vero or Vero E6 cells have been used. Additionally it is also possible to use a fluorescently-labeled specific antibodies for confirmation of antigens in infected cells. Electron microscopy has also been useful in identification and detection of viral infections.[19] The paraffin sections of autopsy material, particularly from the liver and spleen, due to the high condensation of antigens and viral particles, are useful in immune histochemical assays with the use of specific polyclonal or monoclonal antibodies. Formalin-fixed specimens are not infectious and may be sent without special precautions or refrigeration. In some Cases Microarray Techniques are used to Diagnosis of EVD due to its ability to find new strains and multiplexing capacity. Next-generation sequencing (NGS) techniques is powerful tool which allow screening of pathogens and provide proper genome data. NGS methods may be useful to detect Ebola virus in situations where the clinical index of suspicion is not high or where there is low urgency for diagnostic information.

Treatment

First case of EVD in Guinea was reported in March 2014 by World Health Organization, according to the outbreak has continued through the year and the total number of 28,637 patients was reported as the suspected in the EVD-affected countries. Among the cases, 11,315 patients were reported death by 27 December 2015. Proper Vaccines is not developed yet while viral diagnostic methods were already developed and established in a developed countries. Vaccine and therapeutic development is play vital role to stop the EVD and protect the world from the risk which can be generated by spread of Ebola virus. There were no specific vaccine and no successful antiviral drug was available for preventing Ebola virus infection.[22-26]

Drug and Vaccine Development

Drug development for the Ebola disease treatment started in 2002 just after 9/11 in United States, and it was supported by governmental institutes such as National Institute of Health, Some drugs are acts against EVD but still under clinical trials (Table 1) Vaccine were tested at the preclinical levels using Non–Human Primates, and the development of manufacturing process was unpredictable step for the most potentially harmful pathogens such as filovirus including Ebola virus.[28-38] There is also a need to increase health workers' understanding on Ebola disease to improve healthcare like any other viral disease.[39]

CONCLUSION

Ebola virus infection has been a serious threat to human individuals due to its highly infectious and lethal behaviour since it was discovered in 1976. For Ebola hemorrhagic fever no FDA approved medicine or antivirual drugs. The spreading of disease mainly through the transmission of blood and body fluids from one person to another person and some evidence of sexual transmission are found. There is an immediate requirement perfect Molecular diagnostics of diseases. To minimize the Ebola epidemic cases is to

control the spread of the disease. Researcher investigates verity of Antiviral Drugs and Vaccines which are affordable and easily available medication for the treatment of Ebola.

ACKNOWLEDGEMENTS

It would be great to give sincere gratitude & thanks to the Prof. Jurgelevičius and entire team of Dept of Biology, Vytautas Magnus University For proper Guidance. Also very thankful to all those who have help directly or indirectly to carry out the review work successfully.

CONFLICT OF INTEREST

None.

REFERENCES

1. Isaacson M, Sureau P, Courteille G, Pattyn SR. Clinical Aspects of Ebola Virus Disease at the Ngaliema Hospital, Kinshasa, Zaire, 1976.
2. WHO. Media Centre. Ebola virus disease. Fact sheet N°103. Available at: http://www.who.int/mediacentre/ factsheets/fs103/en/ [Accessed September 1, 2015]
3. WHO Global Alert and Response. Ebola Reston in pigs and humans in the Philippines, Available at: www. who.int/csr/don/2009_03_31/en/ [Accessed September 1, 2015]
4. Hawkes N. Ebola outbreak is a public health emergency of international concern, WHO warns. BMJ. 2014;349(9):5089. http://dx.doi.org/10.1136/bmj.g5089
5. Weik M, Enterlein S, Schlenz K, Mühlberger E. The Ebola virus genomic replication promoter is bipartite and follows the rule of six. J Virol. 2005;79(16):10660-71.
6. Fauquet CM, Mayo MA, Maniloff J, Desselberger U, Ball LA. Virus taxonomy: VIIIth report of the International Committee on Taxonomy of Viruses. Academic Press. 2005.
7. Mehedi M, Groseth A, Feldmann H, Ebihara H. Clinical aspects of Marburghemorrhagic fever. Future Virol. 2011;6(9):1091-106.
8. Cases of Ebola virus infection can be exported any old time. Available at: http://virologydownunder.blogspot.com.au/2015/02/cases-of-ebola-virus-infection-can-be.html [Accessed September 1, 2015]
9. Siegert R, Shu HL, Slenczka W, Peters D, Muller G. [On the etiology of an unknown human infection originating from monkeys]. Dtsch Med Wochenschr. 1967;92(51):2341-3.
10. Le Guenno B, Formenty P, Wyers M, Gounon P, Walker F, Boesch C. Isolation and partial characterisation of a new strain of Ebola virus. Lancet. 1995;345(8960):1271-4.
11. Groseth A, Feldmann H, Strong JE. The ecology of Ebola virus. Trends Microbiol. 2007;15(9):408-16.
12. Mate SE, Kugelman JR, Nyenswah TG, Ladner JT, Wiley MR, Cordier-Lassalle T. Molecular Evidence of Sexual Transmission of Ebola Virus. N Engl J Med. 2015;373(25):2448-54.
13. Muyembe-Tamfum JJ, Mulangu S, Masumu J, Kayembe JM, Kemp A, Paweska JT. Ebola virus outbreaks in Africa: past and present. Onderstepoort J Vet Res. 2012;79(2):45.
14. Feldmann H, Geisbert TW. Ebola haemorrhagic fever. Lancet. 2011;377(9768):849-62.
15. WHO risk assessment ,human infection with Zaire ebola virus in west Africa 2014 June 24.
16. Baron RC, McCormick JB, Zubeir OA. Ebola virus disease in southern Sudan: hospital dissemination and intrafamilial spread. Bull World Health Organ. 1983;61(6):997-1003.
17. Wang YP, Zhang XE, Wei HP. Laboratory detection and diagnosis of filoviruses. Virol Sin. 2011;26(2):73-80.
18. Goeijenbiar M,Van Kampem JJ, Reusken CB. Ebola virus diseases: A review on epidemiology, symptoms, treatment and pathogenesis. J Med. 2014;72(9):442-8.
19. Ramanan P, Shabman RS, Brown CS. Filoviral immune evasion mechanisms. Viruses. 2011;3(9):1634-49.
20. Sanchez A, Giesbert TW, Feldmann H. Filoviridae: Marburg and Ebola viruses. In: Knipe DM, Howley PM, Griffin DE, Lamb RA, Martin MA, Roizman B, Straus SE, editors. Fields virology. 5th ed. Philadelphia: Lippincott Williams and Wilkins; 2007, p. 1409-48.
21. Woo YC, Kee-Jong H, Joo EH, Won-Ja Lee. Progress of vaccine and drug development for Ebola preparedness, Clin Exp Vaccine Res. 2015;4(1):11-6
22. Schieffelin JS, Shaffer JG, Goba A, Michael G, Gire SK, Colubri A, et al. Clinical illness and outcomes in patients with Ebola in Sierra Leone. N Engl J Med. 2014;371(22):2092-100
23. Chertow DS, Kleine C, Edwards JK, Scaini R, Giuliani R, Sprecher A. Ebola virus disease in West Africa-clinical manifestations and management. N Engl J Med. 2014;371(22):2054-7.
24. Fowler RA, Fletcher T, Fischer WA, Lamontagne F, Jacob S, Brett-Major D. Caring for critically ill patients with Ebola virus disease. Perspectives from West Africa. Am J Respir Crit Care Med. 2014;190(7):733-7.
25. Plachouras D, Monnet DL, Catchpole M. Severe Ebola virus infection complicated by gram-negative septicemia. N Engl J Med. 2015;372(14):1376-7.
26. Qiu X, Wong G, Audet J, Bello A, Fernando L, Alimonti JB. Reversion of advanced Ebola virus disease in nonhuman primates with ZMapp. Nature. 2014;514(7520):47-53.
27. Vanderzanden L, Bray M, Fuller D, Roberts T, Custer D, Spik K. DNA vaccines expressing either the GP or NP genes of Ebola virus protect mice from lethal challenge. Virology. 1998;246(1):134-44
28. Hoenen T, Groseth A, Feldmann H. Current ebola vaccines. Expert Opin Biol Ther. 2012;12(7):859-72.
29. Takada A. Filovirus tropism: cellular molecules for viral entry. Front Microbiol. 2012;6(3):34.
30. Falzarano D, Geisbert TW, Feldmann H. Progress in filo-virus vaccine development: evaluating the potential for clinical use. Expert Rev Vaccines. 2011;10:63-77.
31. Warfield KL, Goetzmann JE, Biggins JE. Vaccinating captive chimpanzees to save wild chimpanzees. Proc Natl Acad Sci USA. 2014;111(24):8873-6.
32. Geisbert TW, Feldmann H. Recombinant vesicular stomatitis virus-based vaccines against Ebola and Marburg virus infections. J Infect Dis. 2011;204(3):S1075-81.
33. Bishop BM. Potential and emerging treatment options for Ebola virus disease. Ann Pharmacother. 2015;49(2):196-206.
34. Choi JH, Croyle MA. Emerging targets and novel approaches to Ebola virus prophylaxis and treatment. Bio Drugs. 2013;27(6):565-83.
35. WHO. Potential Ebola therapies and vaccines.2014. Available at: http://www.who.int/csr/resources/ publications/ebola/potential-therapies-vaccines/en/ [Accessed September 1, 2015]
36. Gulland A. Clinical trials of Ebola therapies to begin in December. BMJ. 2014;349(14):g6827.
37. Iversen PL,Warren TK,Wells JB,GarzaNL, Mourich DV, Welch LS. Discovery and early development of AVI-7537 and AVI-7288 for the treatment of Ebola virus and Marburg virus infections. Viruses. 2012;4(11):2806-30.
38. Warren TK, Wells J, Panchal RG, Stuthman KS, Garza NL, Van Tongeren SA. Protection against filovirus diseases by a nove lbroad-spectrum nucleoside analogue BCX4430. Nature. 2014;508(7496):402-5.
39. Ahmad A, Khan MU, Gogoi LJ, Kalita M, Sikdar AP, Pandey S. Japanese Encephalitis in Assam, India: Need to Increase Healthcare Workers' Understanding to Improve Health Care. PLoS One. 2015;10(8):e0135767.

Cite this article as: Mali A, Mali DS, Bodake SM, Vaclovas J. Past, Present and Future about Ebola Virus Diseases: An Updated Review. J Pharm Pract Community Med. 2016;2(2):35-39.