



Review Article

A REVIEW ON EBOLA VIRUS, THE DISEASES, CAUSES AND MANAGEMENT

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ABSTRACT

Ebola virus diseases (EVD) is a painful reminder as an outbreak anywhere which can be a risk everywhere. The Global Health Security Agenda pursue to enforce public health systems in most affected countries to eliminate the spreads before they become emergencies. Hemorrhagic fever occurs in less than half of patients and it takes place most commonly in the gastrointestinal tract. The symptoms progress over the time and patients suffer from dehydration, stupor, confusion, hypotension, multi-organ failure, leading to fulminant shock and eventually death. Preclinical evaluation is also underway for various vaccine candidates. It has been hypothesized that infection of macrophages is one of the causes for development of hemorrhage. The objective of the proposed work is to review out the reason and management of Ebola virus and communicating clear and accurate information to all stakeholders including the general public which is the need of the hour.

Keywords: Ebola virus, hemorrhagic fever, outbreak, diseases, management.

INTRODUCTION

Ebola virus disease (EVD) is also known as Ebola hemorrhagic fever (EHF). As the name implies, it causes abnormal bleeding inside and outside of the body, affecting humans and other primates. Ebola disease is caused by an infection with a virus, which is named after a river in the Democratic Republic of the Congo (formerly Zaire) in Africa, where it was first recognized. It originates from the genus Ebola with family *Filoviridae* (order Mononegavirales), according to the International Committee on Taxonomy of Viruses¹. EHF is an acute viral syndrome with fever and subsequent bleeding diathesis marked by high mortality in human and nonhuman primates (monkeys, gorillas and chimpanzees). EHF is caused by any of five genetically different members of the *Filoviridae* family.

- 1) Zaire ebolavirus (ZEBOV)
- 2) Sudan ebolavirus (SEBOV)

- 3) Ivoire ebolavirus
- 4) Bundibugyo ebolavirus (BDBV)
- 5) Reston ebolavirus (REBOV).

Ivoire ebolavirus has been accompanied with only one human case². REBOV has only caused disease in non-human primates (NHP) and was found in swine suffering from porcine reproductive and respiratory disease syndrome. It 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 died¹.

Zaire, Sudan and Bundibugyo Ebola viruses are accountable for most of the EHF epidemic but ZEBOV establish a particularly serious threat to both human and NHPs in sub-Saharan Africa. Ebola virus disease (EVD) is a severe, often fatal illness in humans. EVD outbreaks have a case fatality rate of up to 90%¹.

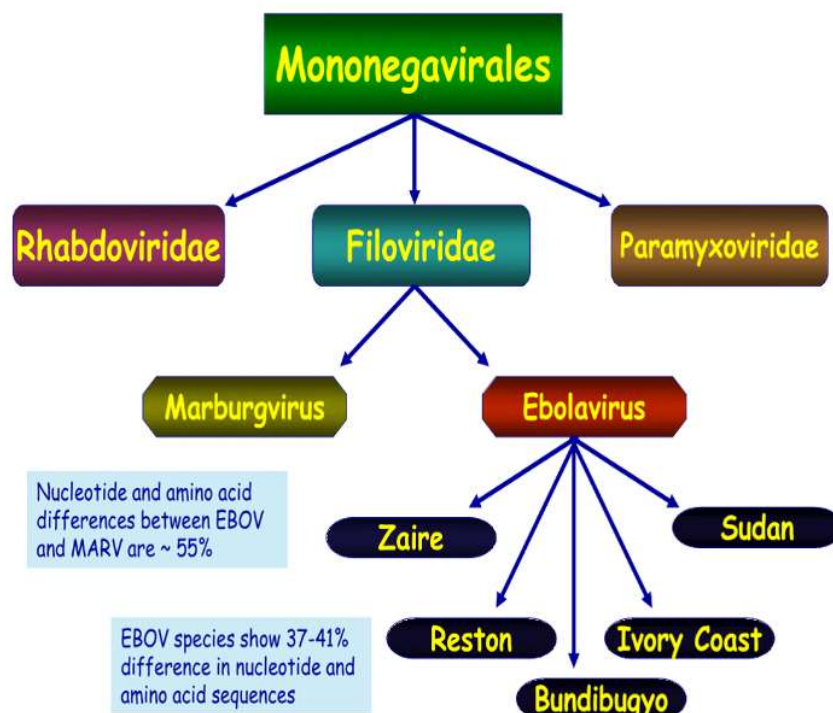


Figure 1: Taxonomy of Filovirus

Types of Ebola Virus

Ebola haemorrhagic fever (EHF) is caused by any of above five genetically distinct members.

1. Ebola virus or Zaire Ebola virus (EBOV)

This is most fatal among all five and has the highest case-fatality rate, upto 90% in some epidemics. The symptoms of Zaire Ebola virus has like malaria and patients are sometimes treated with quinine. The transmission of virus was to be due to reuse of the needle for Lokela's injection without sterilization. Concurrent transmission was also due to the traditional interment preparation method, which involves washing and gastrointestinal tract cleansing³. Zaire Ebola virus has been associated with only one human case.

2. Sudan virus (SUDV)

The virus also caused threaten effects to the people who's was working in cotton factory in Nzara, Sudan, with the first case reported as a worker exposed to a potential natural reservoir⁴.

3. Tai Forest virus (TAFV)

Also referred to as Ivory Coast Ebola virus and Tai Ebola virus; it was first discovered among chimpanzees from the Tai Forest in Cote d'Ivoire, Africa. The source of contamination was believed to be the meat of infected Western Red Colobus monkeys, upon which the chimpanzees preyed. One of the scientists performing the necropsies on the infected chimpanzees contracted Ebola⁵.

4. Bundibugyo virus (BDBV)

BDBV is a close relative of the much more commonly known Ebola virus (EBOV). The name BDBV is originated from *Bundibugyo* which is the name of the one of the town of Ugandan Bundibugyo District, where it was first discovered⁶.

5. Reston virus (RESTV)

It is not thought to be disease-causing in humans. It is non-pathogenic to humans however hazardous in monkeys. Reston Ebola virus disease has found in non-human mammals and was also in swine suffering peoples with reproductive and respiratory disease syndrome. EHF typically appears in sporadic outbreaks coinciding with the rainy season, and is usually spread in humans within a health-care setting⁷.

History

Ebola virus was first well-known in 1976 when an onset of Ebola hemorrhagic fever developed in Zaire and another later that year in Sudan. The Zaire Ebola virus has one of the highest virulence rates of virus affecting humans. In the 1976, Ebola virus killed 88 percent of patients, 81 percent in 1995, 73 percent in 1996, 80 percent in 2001, 2002, and 90 percent in 2003, although none of these outbreaks were as large as the original.

Sudan Ebola virus has a lower, yet still very dangerous, fatality rate of 53 percent in 1976, 65 percent in 1979, 53 percent in the over 400 patients infected in 2000, and 41 percent in 2004. Ivory Coast Ebola virus was first identified in 1994 when a scientist carried out dissection on chimpanzees deflated Ebola hemorrhagic fever. Most Ebola virus outbreaks have originated in Africa and have traveled only to other countries through freight of non-human mammals or through accidental contamination in testing facilities^{8,9}.

Prevalence

Ebola virus refined in 1976 in Sudan, Nzara, Yambuku with Democratic Republic of Congo^{10,11}. World Health Organization characterizes a dominant Ebola smash in Sierra Leone western African nations, Liberia, Guinea in March 2014. The 2014

convulsion of diseases in West Africa begin by Zaire Ebola virus is the protracted, greatest and tealest in history.

There were 22,859 EVD cases and approximately 9,162 deaths as of 11 February 2015 compared to the cumulative sum of past episodes in 36 years (1976-2012), and over six times the total number of mortality^{12, 13, 14}.

From 1976 to December 2012, there was 23 outbreaks of Ebola have been summarized; during these events a total of 2388 Ebola cases including 1590 deaths were reported¹⁵.

Since its discovery in 1976, Ebola virus disease (EVD) has mostly occurred in sub-Saharan Africa.

Research have based upon serological confirmation of Ebola virus infection in orangutans in Indonesia¹⁶ in several bat species in China¹⁷ and in Rousettus leschenaultia fruit bats, Bangladesh¹⁸.

Table 1: Prevalence of Ebola virus diseases in different countries

Country	Total Cases	Laboratory Confirmed Cases	Death
Guinea	2292	2051	1428
Liberia	7719	2830	3177
Sierra Leone	7897	6375	1768
Nigeria	20	19	8
United state	4	4	1
Spain	1	1	0

Onset

EVD has an incubation period of 2 to 21 days before the onset of symptom. Incubation period is last for 4 to 10 days¹⁹.

Symptom

Bleeding: All people infected show some symptoms of circulatory system like impaired blood clotting, in 40–50% bleeding from puncture sites and mucous membranes (e.g. mouth, gastrointestinal tract, nose, ears, vagina and gums), reddening of eyes and bloody vomit has also been reported²⁰⁻²⁴.

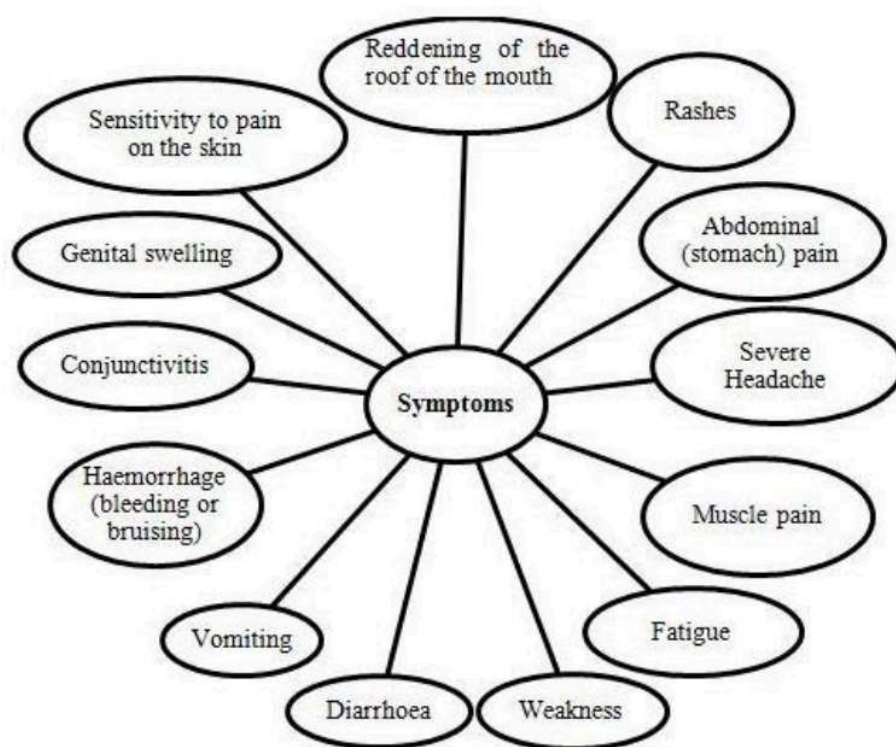


Figure 2: Symptoms of Ebola

Epidemiology

Ebola virus disease is a zoonotic disease and each outbreak in the human population is started by an entrance from an animal inventory i.e. due to hunting, direct contact with infected animals, gripping of bush meat²⁵. A principal origin of infection

is direct contact with a sick person, or when viral infection is in the highest point or when contaminated objects used by the patient. Body fluids and secretions mainly blood, saliva, urine, vomit, feces, semen are infectious. Filoviruses enter the host through mucosal surfaces, breaks, and abrasions in the skin²⁶.

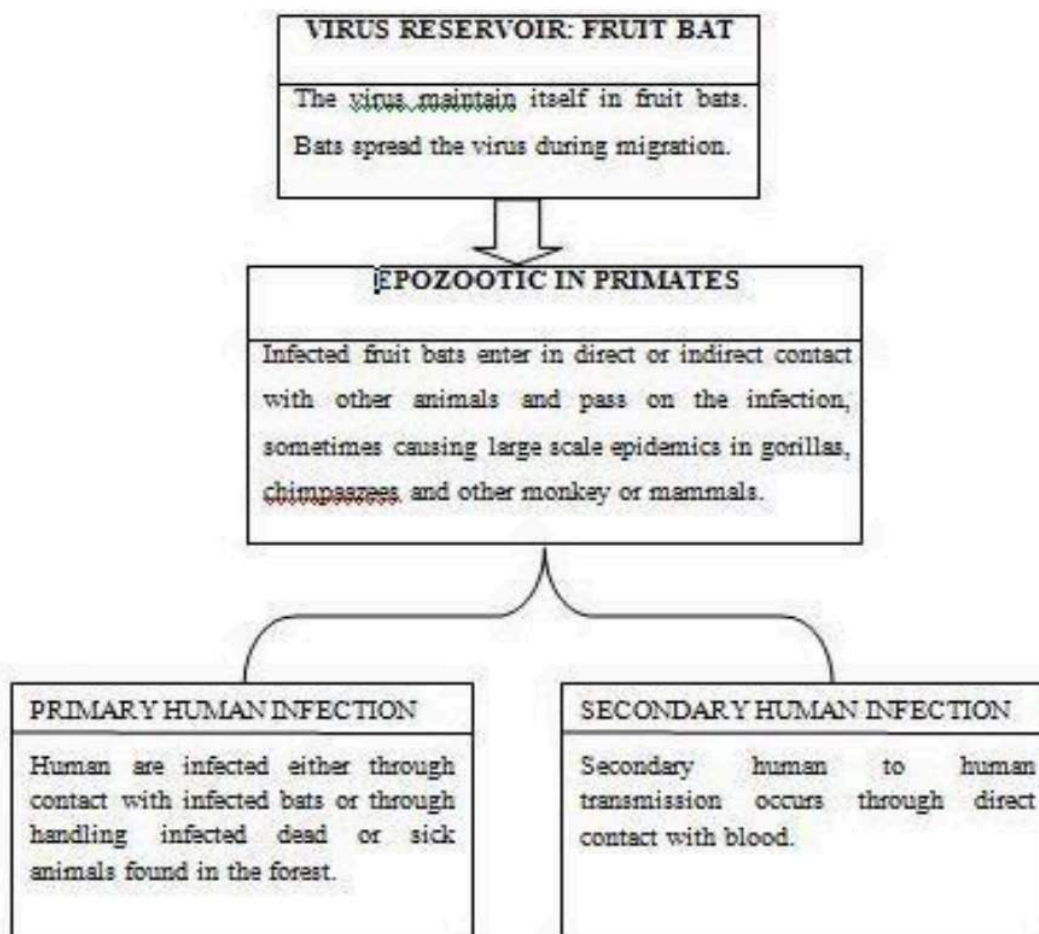


Figure 3: Mode of Transmission of Ebola

Pathophysiology of Ebola virus disease

The natural reservoir host of Ebola virus is fruit bats, which belong to Pteropodidae family, and accidental hosts are humans and non-human primates. These viruses remain in nature prior to vast natural or human made environmental changes, relevance elements or ecologic conditions enable them to remerge²⁷. Bats and apes proceed entry of filovirus in the human is interfere by the viral stick glycoprotein, which attaches the viral particles to the cell surface²⁸. The chief feature of epidemics is human to human transmission. Direct infection of monocytes and macrophages causes the release of cytokines leading to inflammation and fever, which causes to host immune responses to Ebola virus and damage of the cell²⁹.

After access in human body, EBOV mainly effects on lymph nodes, Liver and Adrenal gland.

- Lymph nodes: EBOV causes infection of macrophages and dendritic cells. They lead to depletion of lymphocytes and impairment in host immune response.
- Liver: In liver, it causes infection and necrosis of hepatocytes through the damage of the endothelial cells. The formation of the lining of the blood vessels has carried out. There was difficulty in coagulation of the infected individual's blood. As the platelets would not be able to coagulate, this result in hypovolemic shock or decrease in blood pressure and death may also occur.
- Adrenal gland: In Adrenal gland it causes infection and necrosis of adrenal cortical cells. Due to which synthesis of steroids is impaired.

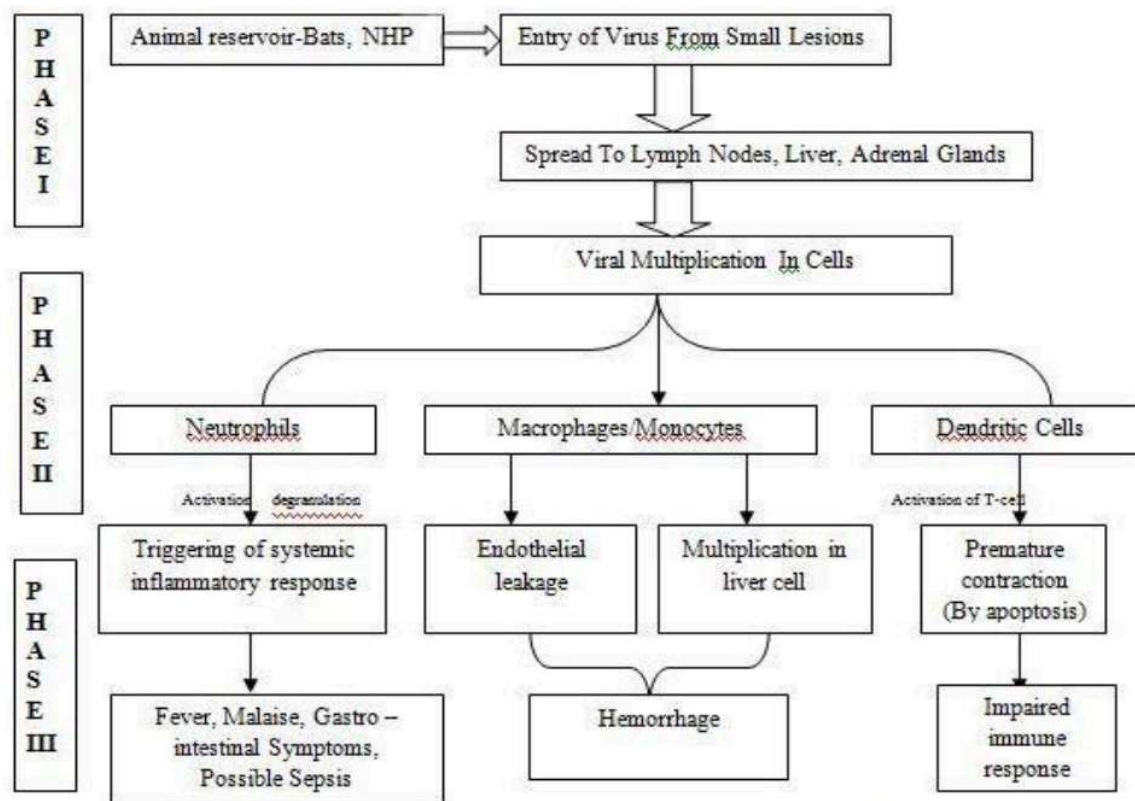


Figure 4: Pathophysiology of Ebola Virus Disease

Diagnosis of EVD

Following laboratory tests are used for the diagnosis of Ebola virus infections^{30, 31, 32}.

Table 2: Laboratory test for diagnosis of EVD

Antigen detection tests	Kidney function test
Serum neutralization test	Electrolytes
RT-PCR assay	WBC
Virus isolation by cell culture	Repeated platelet count
Haematocrit	Hemoglobin
ELISA	Liver function test

Management considerations for EVD³³

There are seven steps for the management of EVD that are given below:

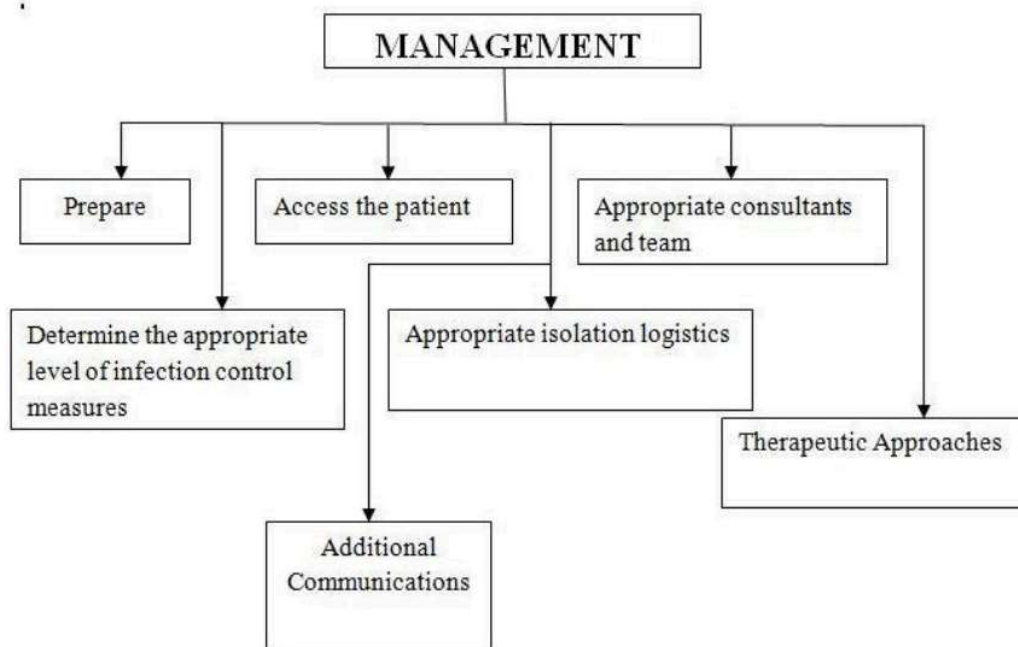


Figure 5: Management of Ebola virus

Therapeutic approaches & treatment of EVD

There is no particular drugs and treatment for EVD. The treatment is mainly based on supportive and symptomatic remedy focusing on supplying proper hydration and nutritional support with antibiotics, control of organ failure, and Antimalarial drugs if required³⁴.

Table 3: Therapeutic Approaches & Treatment of EVD^{24, 35, 36, 37}.

Sr. no	Agent	Manufacturer	Stage of evaluation
1	TKM-Ebola	Tekmira, Canada	Phase I
2	Favipiravir (T-705)	Institute National, France	Phase II, protective in mouse model
3	CMX001 (Brincidofovir)	Chimerix, Durham	Phase II
4	JK-05	Sihuan Pharmaceutical Ltd China	Animal studies; Use in emergency situations for army only
5	BCX4430	BioCryst Pharmaceuticals, Durham	Phase I
6	Anti-Ebola hyperimmune globulin	None identified	Animal studies
7	ZMapp	National Institute of Allergy and Infectious Diseases NIAID	Phase I/II
8	ChAd3-EBOZ	GlaxoSmithKline, National Institutes of Health	Phase I
9	rVSV-EBOV: recombinant vesicular stomatitis virus	New Link Genetics	Efficacy in rodents and nonhuman primates
10	Human adenoviruses 25 and 35 and MVA vectors	Johnson & Johnson, New Brunswick, Bavarian Nordic, Kvistgaard, Denmark	Rodents and nonhuman primates. Phase I trials.
11	Recombinant protein- Ebola glycoprotein	Protein Sciences	Efficacy in rodents.
12	EBOV GP Vaccine	Novavax, Gaithersburg	Preclinical studies; Nonhuman primate study
13	Oral Ad5: Oral tablet vaccine based on human adenovirus	Vaxart, South San Francisco	Protective against challenge in preclinical studies
14	rVSV-EBOV	Profectus Biosciences, Baltimore	Vaccine component expressing HIV gag.
15	DNA-EBOV	Inovio, San Diego, Calif	Phase I
16	Recombinant rabies EBOV	National Institutes of Health	Phase I
17	FGI-103	Recirca, Inc. (Painesville)	Protects mice with delayed cytokine response
18	TKM-Ebola	Tekmira Pharmaceuticals Corporation, Vancouver, Canada	Provided 100% survival in monkey
19	AVI-7537	Sarepta Therapeutics, Cambridge, MA, USA	Suppresses disease in mice and NHPs
20	BCX4430	BioCryst Pharmaceuticals	Inhibits infection in vitro
21	Clomiphene & Toremiphene	Inter Steroids Pharmaceutical Co, Ltd, Hangzhou, China	Inhibits virus entry in vitro in Vero E6 and HepG2 cell lines

RECOMMENDATIONS AND CONCLUSION

Ebola has been a hazard to human health due to terrible, highly virulent and contagious behavior since its discovery in 1976. Ebola fever has come out as one of the most fatal identified forms of hemorrhagic fever which causes higher number of mortality and morbidity rate. The transmission surrounding humans occurs mainly through the exchange of blood and body secretions. Other noticeable forms of expansion comprise hospital acquired infection and inadequate hygiene condition. There is an urgent requirement of dissemination of information to community and training programmes for doctors, nurses and other hospital staff. The future endeavors require the priority on the understanding of the differences among species of ebola virus. The best method to lower the cases and epidemic is to prevent the spread of the disease. The awareness programmes should be organized on large scale to develop the attentiveness about disease for its eradication. Although great improvements have been achieved over the past decade, better surveillance, real-time sharing of data and taking rapid action based on the available information remain necessary. Because Ebola virus is primarily transmitted through contact with the body fluids of symptomatic patients, the infection spread can be stopped by an early diagnosis, contact tracing, patient isolation and care, infection control and safe burial. Many factors are responsible for Ebola Epidemic. The time period for the aggression of virus and its symptoms has up to twenty-one days.

REFERENCES

- Gatherer D. The Ebola virus disease outbreak in west Africa. *Journal of General Virology* 2014; 95: 1619–1624.
- Mittal V, Chhabra M & Venkates S. Ebola Virus - An Indian Perspective. *The Indian Journal of Pediatrics* 2015; 1-3. Available at: <https://www.researchgate.net/publication/272193337>.
- Johnson KM, Webb PA, Lange JV, Murphy FA. Isolation and characterization of a new virus (Ebola virus) causing acute hemorrhagic fever in Zaire. *The Lancet* 1977; 1:569–71.
- Ebola haemorrhagic fever in Sudan, 1976. Report of a WHO/ International Study Team. *Bulletin of World Health Organization* 1978; 56:247–70.
- Kuhn JH, Becker S, Ebihara H, Geisbert TW, Kawaoka Y, Netesov SV, Nichol ST, Peters CJ, Volchkov VE, Jahrling PB *et al.* Proposal for a revised taxonomy of the family Filoviridae: classification, names of taxa and viruses, and virus abbreviations. *Archives of Virology* 2010; 155(12): 2083–2103.
- Smith DH, Johnson BK, Isaacson M, Swanapoel R, Johnson KM, Killey M, Bagshawe A, Siongok T, Keruga WK *et al.* Marburg virus disease in Kenya. *Lancet* 1982; 1(8276):816–20.
- Barrette RW, Metwally SA, Rowland JM, Xu L, Zaki SR, Nichol ST, Rollin PE, Towner JS, Shieh W-J, Batten B, Sealy TK, Carrillo C, Moran KE, Bracht AJ, Mayr GA, Sirios-Cruz M, Catbagan DP, Lautner EA, Ksiazek TG, White WR, McIntosh MT *et al.* Discovery of Swine as a host for the Reston ebola virus. *Science* 2009; 325:204–206.
- Karunakar T, Kumar E, Naresh K, Sriram R. A review on Ebola virus. *International Journal of Pharmacotherapy* 2013; 3(2): 55-59.
- Peters CJ, LeDuc JW. An introduction to Ebola: the virus and the disease. *Journal of Infection* 1999; 179 (1): 9-16.
- Baron RC, McCormick JB, Zubeir OA. Ebola virus disease in southern Sudan: hospital dissemination and intrafamilial spread. *Bulletin of the World Health Organization* 1983; 61(6):997-1003.
- Ebola haemorrhagic fever in Zaire, 1976. Report of a WHO/ International Study Team. *Bulletin of World Health Organization* 1978; 56: 271–93.
- Shears P, O'Dempsey TJ. Ebola Virus Disease in Africa: Epidemiology and nosocomial transmission. *Journal of hospital infection* 2015; 90(1): 1-9.
- Meltzer MI, Atkins CY, Santibanez S Barbara Knust, Petersen BW, Ervin ED, Nichol ST
- Damon IK, Washington ML *et al.* Estimating the future number of cases in the Ebola epidemic: Liberia and Sierra Leone, 2014–2015. *Morbidity and Mortality weekly report Surveillance Summary* 2014; 63(3):1–14.
- Gostin LO, Friedman EA. A retrospective and prospective analysis of the west African Ebola virus disease epidemic: robust national health systems at the foundation and an empowered WHO at the apex. *Lancet* 2015; 385: 1902-1909.
- Nidom CA, Nakayama E, Nidom RV, Alamudi MY, Daulay S, Dharmayanti IN, Dachlan YP, Amin M, Igarashi M, Miyamoto H, Yoshida R, Takada A *et al.* Serological evidence of Ebola virus infection in Indonesian orangutans. *Public Library of Science One* 2012; 7(7):1-7.
- Yuan J, Zhang Y, Zhang Y, Wang LF, Shi Z. Serological evidence of Ebolavirus infection in bats, China. *Virology Journal* 2012; 9:236.
- Olival KJ, Islam A, Yu M, Anthony SJ, Epstein JH, Khan SA, Khan SU, Crameri G, Wang L, Lipkin WI, Luby SP, and Daszak P *et al.* Ebola virus antibodies in fruit bats, Bangladesh. *Emerging Infectious Diseases* 2013; 19(2):270-273.
- Negredo A, Palacios G, Vazquez-Moron S, Gonzalez F, Dopazo H, Molero F, Juste J, Quetglas J, Savji N, Martinez MC, Herrera JE, Pizarro M, Hutchison SK, Echevarria JE, Lipkin WI, Tenorio A *et al.* Discovery of an Ebolavirus-like filovirus in Europe. *PLoS Pathog* 2011; 7(10):e1002304.
- Cases of Ebola Diagnosed in the United States. Centers for Disease Control and Prevention (USA). Available at: <http://www.cdc.gov/vhf/ebola/> October 2014.
- Sunitha D, Chary MN, Hemalatha K, Unissa R. Prevention Of Ebola Virus Disease-A Review. *European Journal of Pharmaceutical and Medical Research* 2015; 2(6): 276-282.
- Carette JE, Raaben M, Wong AC. Ebola virus entry requires the cholesterol transporter Niemann-Pick C1. *Nature* 2011; 477(7364): 340–3.
- West TE, Arnim VSAV. Clinical presentation and management of severe Ebola Virus disease. *Annals of American Thoracic Society* 2014; 11(9):1341–1350.
- Cote M, Misasi J, Ren T, Bruchez A. Small molecule inhibitors reveal Niemann-Pick C1 is essential for Ebola virus infection. *Nature* 2011; 477(7364): 344–8.
- Kilgore PE, Grabenstein JD, Salim AM, and Rybak M. *Pharmacotherapy* 2015; 35:43-53.
- Colebunders R, Borchert M. Ebola haemorrhagic fever-a review. *Journal of Infection* 2000; 40(1): 16-20.
- Zawilińska BB, Vnenchak MK. General introduction into the Ebola virus biology and disease. *Folia medica cracoviensia* 2014; 3:57–65.
- Sullivan N, Yang ZY, Nabel GJ. Ebola virus pathogenesis: implications for vaccines and therapies. *Journal of Virology* 2003; 77:9733-9737.
- Connolly BM, Steele KE, Davis KJ, Geisbert TW, Kell WM, Jaax NK, Jahrling PB *et al.* Pathogenesis of experimental Ebola virus infection in guinea pigs. *Journal of Infectious Diseases* 1999; 179(1): 203-217.
- Carette JE, Raaben M, Wong AC, Herbert AS, Obernosterer G, Mulherkar N, Kuehne AI, Kransusch PJ, Griffin AM, Ruthel G, Dal Cin P, Dye JM, Whelan SP, Chandran K, Brummelkamp TR *et al.* Ebola virus entry requires the

- cholesterol transporter Niemann Pick C1. *Nature* 2011; 477(7364):340-343.
31. Kortepeter MG, Bausch DG, Bray M. Basic clinical and laboratory features of filoviral hemorrhagic fever. *Journal Infectious Diseases* 2011; 204(3):810–816.
 - Ksiazek TG, Rollin PE, Williams AJ, Bressler DS, Martin ML, Swanepoel R, Burt FJ, Leman PA, Khan AS, Rowe AK, Mukunu R, Sanchez A, Peters CJ et al. Clinical virology of Ebola Hemorrhagic Fever (EHF): virus, virus antigen, and IgG and IgM antibody findings among EHF patients in Kikwit, Democratic Republic of the Congo, 1995. *Journal of Infectious Diseases* 1999; 179(1):177-87.
 32. Grolla A, Lucht A, Dick D, Strong JE, Feldmann H. Laboratory diagnosis of Ebola and Marburg hemorrhagic fever. *Bulletin Society of Pathology Exotique* 2005; 98:205-9.
 33. Kortepeter MG, Martin JW, Rusnak JM, Cieslak TJ, Warfield KL, Anderson EL and Ranadive MV et al. Managing potential laboratory exposure to Ebola virus by using a patient biocontainment care unit. *Emerging Infectious Diseases* 2008; 14(6):881-887.
 34. Rajak H, Jain D K, Singh A, Sharma AK, Dixit A. Ebola virus disease: past, present and future. *Asian Pacific Journal of Tropical Biomedicine* 2015; 5(5): 337-343.
 35. Geisbert TW, Pushko P, Anderson K, Smith J, Davis KJ, Jahrling PB. Evaluation in nonhuman primates of vaccines against Ebola virus. *Emerging Infectious Diseases* 2002; 8: 503–07.
 36. Huggins J, Zhang ZX, Bray M. Antiviral drug therapy of filovirus infections: S-adenosylhomocysteine hydrolase inhibitors inhibit Ebola virus in vitro and in a lethal mouse model. *Journal of Infectious Diseases* 1999; 179 (1): 240–247.
 37. Haque A, Hober D, Blondiaux J. Addressing Therapeutic Options for Ebola Virus infection in Current and Future Outbreaks. *Antimicrobial Agents Chemotherapy* 2015; 59: 5892-5902.

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