EBOLA VIRUS DISEASE: A REVIEW

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ABSTRACT
Background: Ebola virus (EBV) is a member of the family, Filoviridae, and is the etiological agent of Ebola virus disease or Ebola hemorrhagic fever (EHF). This disease causes significant morbidity and mortality in humans and non-human primates, with human fatality rates reaching 90% during outbreaks. EVD is presently one of the world's feared, and classified as a biological class 4 pathogen and its natural reservoir is not known. This review describes the epidemiology, clinical features diagnosis and treatment of EVD. The understanding of viral pathogenesis is limited. Therefore, further studies examining the pathogenic mechanisms of EBV are necessary to fully understand and effectively treat EVD.
Aim: The aim of this review is to obtain information on Ebola virus disease, its Virology, pathogenesis, immune response and immune response evasion as well as some current diagnosis approaches.
Conclusion: EVD is presently one of the world's feared, and classified as a biological class 4 pathogen with its natural reservoir not known, it has been a serious threat to human individuals due to its highly infectious and lethal behavior, Since the spreads of the disease is mainly through the transmission of blood and body fluids from infected person Extra care should be observed, since yet no approved specific vaccine or antiviral drug to treat the infection.
Key Words: Ebola virus Disease, Ebola hemorrhagic fever.

INTRODUCTOIN

Ebola virus (EBV) causes fatal infection in human known asEbola virus disease (EVD) or Ebola hemorrhagic fever (EHF) which may show multiple, serial, and nonspecific-disease, symptoms including high fever, headache, vomiting, anorexia, diarrhea, muscles ache, unexplained bleeding in the eyes, nose, gums, and gut occurs in the advanced stages (Feldman *et al*., 2013). The first outbreak of EVD was reported in 1976 in the Democratic Republic of the Congo, since then, there have been reports of small EVD outbreaks in some countries in Central Africa, including Sudan and Uganda (Hirokazu *et al*., 2015).

The 2014–2015 Ebola outbreak which is the largest in history is a clear evidence of this, as the outbreak went beyond the traditional East Africa countries of previous outbreaks and spread to
Nigeria, Spain, United States of America, England and Italy (WHO 2014).

Ebola virus is a non□segmented negative sense single stranded RNA virus belonging to the genus Ebola virus in the family *Filoviridae* (order *Mononegavirales*) which presently consists of three genera; the Ebola virus(EBOV), Marburg virus (MARV) and Cueva virus (WHO 2014).

Five distinct species of the genus Ebola virus are known: Zaire Ebola virus Sudan Ebola virus, Taï forest Ebola virus, Bundibugyo Ebola virus and Reston Ebola virus (Omilabu *et al*., 2016).

Filoviruses are enveloped, non-segmented, negative stranded RNA viruses. The virion comprises a core ribonucleocapsidcomplex surrounded by a lipid envelope which isderived from the host cell plasma membrane (Omilabu*et al*., 2016).The 19 kb noninfectious genome encodes seven structural proteins with the following gene order: 3leader, a nucleocapsidprotein (NP), structural virion protein (VP35),a matrix protein VP40, glycoprotein (GP), two additional structural proteins VP30, VP24, and the RNA-dependent RNA polymerase L protein, and 5'trailer VP24 and

VP35 have been shown to act as interferon antagonists (Kelly and Gene 2011).

The pathogenesis of the disease is still not completely known (Michalek *et al*., 2015). EBOV can enter the host body mostly via mucosal surfaces, or injuries in the skin (Hofmann *et al*., 2012). Also, infection through the intact skin cannot be excluded, although it is considered unlikely (Michalek *et al*., 2015). Aerosol infection (RESTV) has been demonstrated in non-human primatesunder experimental conditions in dispersion chambers (Michalek *et al*., 2015). EBOV infection is characterized by immune suppression and a systemic inflammatory response, which could cause damage of the vascular, and immune systems, that can lead to multiorgan failure and shock (Feldmann and Geisbert 2011). Geisbert et al. presented study in non-human primates and showed that EBOV replicates inmonocytes, macrophages, and dendritic cells; however, in situ hybridization and electron microscopy have also shown the presence of virus in endothelial cells, fibroblasts, hepatocytes, and adrenal cells (Michalek *et al*., 2015). Del Rio et al. demonstrated, the EBOV disseminates to thelymph nodes, liver, and spleen (Michalek *et al*., 2015).

Survivors of filovirus infection have an early and short-lived rise in serum chemokines, indicative of innate immune system induction (Leroy *et al*., 2001 and Wauquier *et al*., 2010). In a recent and relatively large study of EBOV-infected individuals, non survivors develop extremely high levels (5–1000X) of proinflammatory cytokines (IL-1β, IL-1RA, IL-6, IL-8, IL-15, and IL-16) and chemokines (MIP-1α, MIP-1β, MCP-1, MIF, IP-10 GRO-α, and eotaxin) that began rising shortly after disease onset and continuing until the last sampling within 2-3 days before death (Wauquier *et al*., 2010). Interestingly, both survivors and non-survivors do not differ in their serum levels of important regulators of adaptive immunity such as IFN-α, IFN-γ, IL-12, IL-17, or TNF (Wauquier*et al*., 2010). Consistently with these findings, the filoviruses encode interferon antagonists VP24 and VP35, which block interferon production and inhibit downstream interferon signaling (Basler and Amarasinghe, 2009). Filoviruses evade the immune system by preventing the maturation of DC, the cornerstone of innate and adaptive immunity (Mahanty *et al*., 2003). These data suggest that EBOV may block DC maturation after infection, thereby inhibiting activation of lymphocytes and eliminating those subsets that are most likely to be capable of mounting an effective response to the virus (Gupta *et al*., 2001). Activation and maintenance of natural killer (NK) cells appears to be vital to protection against lethal filovirus infection (Warfield *et al*., 2004) however, NK cells and other lymphocytes are depleted during filovirus infection of human and NHPs (Feldmann *et al*., 2007 and Hutchinson and Rolli 2007). The disappearance of NK and T cells in the periphery is presumptively due to apoptosis by a yet unidentified mechanism, although a Fas/FasL interaction is likely involved (Wauquier *et al*., 2010).

individuals who succumb to filovirus infection (EVD) fail to mount a substantial cellular or humoral immune response (Wauquier *et al*., 2010).

In non-survivors, activation of immune cells and secretion of cytokines and chemokines are detected early in infection; however, these early cellular responses appear to be attenuated and are not detectable at the time of death while the levels of proinflammatory cytokines and chemokines reach enormous levels before a fatal outcome (Wauquier*et al*., 2010). Fatal cases of filovirus hemorrhagic fever (EHF) are associated by a marked lack of detectable adaptive immunity (Wauquier*et al*., 2010). After onset of symptoms, a massive loss of CD4+ and CD8+ T cells occurs. In fatal cases of disease, gross numbers of CD4+ and CD8+ T cells are greatly reduced in non-survivors as compared to survivor (6–10% versus 20–40%, respectively (Wauquier *et al.,* 2010).

Filoviral infection also interferes with proper functioning of the innate immune system (Misasi and Sullivan 2014, and Olejnik *et al*., 2011). EBOV proteins blunt the human immune system's response to viral infections by interfering with the cells' ability to produce and respond to interferon proteins such as interferon-alpha, interferon-beta, and interferon gamma (Kühl and Pöhlmann 2012; Romanan *et al*., 2011).

At present, the gold standard for clinical diagnosis of EVDis real-time polymerase chain reaction, antigen detection with an enzyme-linked immunosorbent assay (ELISA) is also used (Fowler *et al*.,2014). The RT-PCR testing of patient samples in the endemic West African areas is being performed in the fieldand, ironically, is sometimes the only laboratory testing available for patients(Fowler *et al*., 2014).

Filovirions, such as EBOV, may be identified by their unique filamentous shapes in cell cultures examined with electron microscopy, but this method cannot distinguish the various filoviruses (Mittal *et al*., 2015).

RECOMMENDATION

Since the virus takes its deadly action in a space of days and weeks which would not reach a month, it is not always possible to identify patients with EBV early because initial symptoms may be non-specific. For this reason, (1) WHO establishes that it is important that health-care workers apply standard precautions consistently with all patients – regardless of their diagnosis – in all work practices at all times. These include basic hand hygiene, respiratory hygiene, and the use of personal protective equipments, safe injection practices and safe burial practices (2) There should be an immediate requirement of conveying the information to the public and conducting training programmes for health care professionals andother hospital staff. (3) More healthcare programmes are required to conduct in a large scale for developing the awareness about Ebola virus disease, its preventive measures and eradication process. (4) Extensive research and investigations are needed to develop an accurate diagnostic procedure as well as an affordable and easily available medication for the treatment of Ebola virus disease. (5) Also, more intensive research should be done by scientists to ascertain more accurately, the actual source of the Ebola virus disease as well as its effect on biodiversity. This will help in defining or streamlining the role people can play in preventing the spread of the virus.

CONCLUSION

EVD is presently one of the world's feared, and classified as a biological class 4 pathogen with its natural reservoir not known, it has been a serious threat to human individuals due to its highly infectious and lethal behavior since it was discovered in 1976. Since the spreads of the disease is mainly through the transmission of blood and body fluids from one person to another due to inadequate hygienic procedures, best method to minimize the Ebola epidemic cases is to control the spread of the disease. Extra care should be observed, since yet no approved specific vaccine or antiviral drug to treat the infection, the above recommendation may help in reducing the burden of the EVD.

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