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Ebola virus disease: past, present and future

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ABSTRACT

Ebola virus disease is one of the most deadly ailments known to mankind due to its high mortality rate (up to 90%) accompanying with the disease. Ebola haemorrhagic fever (EHF) is an infectious disease of animal that can be transmitted to both human and non-human primates. The first epidemic of EHF occurred in 1976 in the Democratic Republic of the Congo. The incubation period of ebola is less than 21 days. Ebola virus infections are depicted by immune suppression and a systemic inflammatory response that leads to damage of the vascular, coagulation and immune systems, causing multi-organ failure and shock. Five genetically distinct members of the *Filoviridae* family responsible for EHF are as follows: *Zaire ebolavirus*, *Sudan ebolavirus*, *Côte d'Ivoire ebolavirus*, *Bundibugyo ebolavirus* and *Reston ebolavirus*. The ongoing 2014 West Africa ebola epidemic has been considered as the most serious panic in the medical field with respect to both the number of human cases and death toll. The natural host for ebola virus is unknown, thus it is not possible to carry out programs to regulate or abolish virus from transmission to people. The ebola virus infection provides little chance to develop acquired immunity causing rapid progression of the disease. It is pertinent to mention that at present, there is no antiviral therapy or vaccine that is helpful against ebola virus infection in humans. The impediment of EHF necessitates much better understanding of the epidemiology of the disease, particularly the role of wildlife, as well as bats, in the spread of ebola virus to humans.

1. Introduction

The new fatal diseases are being continuously reported in the past decade[1]. Ebola virus diseases (EVDs) have always been a challenge and a global menace since its discovery in 1976 by Dr. Peter Piotin in Zaire, Africa (now Democratic Republic of Congo) from the blood of a catholic nun who suspected of having yellow fever[2]. Ebola haemorrhagic fever (EHF) is a zoonotic disease transmitted accidentally by direct contact with infected live or dead animals. 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). Ebola virus is a violent pathogen, a lipid-enveloped negatively stranded RNA virus that belongs to the viral family *Filoviridae*[3]. Exhaustive investigation on EHF in the equatorial region of the Democratic Republic of Congo between 1981 and 1985 pointed out that EHF episodically come out from nature to infected humans[4]. EHF is caused by any of five genetically different members of the *Filoviridae* family: *Zaire ebolavirus* (ZEBOV), *Sudan ebolavirus* (SEBOV), *Côte d'Ivoire ebolavirus*, *Bundibugyo ebolavirus* (BDBV) and *Reston ebolavirus* (REBOV). *Côte d'Ivoire ebolavirus* has been accompanied with only one human case[5]. REBOV has only caused disease in non-human primates (NHP) and was found in swine suffering from porcine reproductive and respiratory disease

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syndrome[6]. 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. EHF has been associated with large human outbreaks, with case fatality rates for ZEBOV as high as 90%[7-9]. The 2014 West Africa ebola outbreak is an ongoing epidemic of the EVD in West Africa. The outbreak began in the republic of Guinea in February of 2014. Since its initial outbreaks, the virus has already spread to the republic of Liberia and the Sierra Leone. The 2014 West Africa Ebola outbreak is believed to be the most terrible in medical history with regards to both the number of human cases and fatalities[10-13]. Presently, there are no approved antiviral drugs or vaccines against filoviruses. The prevention of EHF requires more awareness of the pathology of the ailment, especially the role of wildlife, especially bats, in the spread of Ebola virus to humans. The present review is an attempt to summarize various essential aspects of EVD or EHF.

2. Virology

The EVD, previously known as EHF is a severe condition caused by a virus belonging to genus *Ebolavirus*, family *Filoviridae* and order Mononegavirales. The family *Filoviridae* comprises of one genus, Filovirus, which contains two species, morphologically identical but serologically distinct: Marburg virus and Ebola virus. There are five Ebola subtypes BDBV, ZEBOV, REBOV, SEBOV and *Taï Forest ebolavirus* (TAFV) which vary in pathogenicity, antigenicity and genomic constitution[16]. BDBV, ZEBOV and SEBOV have been accompanied with large EVD epidemic near the tropical rain forests of Central and West African distant villages; among these three ZEBOV are responsible for high mortality rates in humans. REBOV and TAFV were not accustomed for illness or mortality in human. The gene products of ebola and Marburg viruses exhibit a noteworthy degree of similarity and in some areas extensive identity, but are encoded in contradictory nucleotide sequences[17,18](Figure 1).

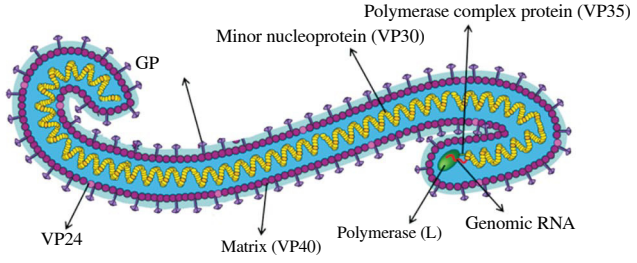

Figure 1. Schematic representation of the ebola virus[14,15,33].
VP: virion protein; GP: glycoprotein.

3. Ecology

Tropical rain forests in Africa provide a general ecosystem for ebola virus emergence, presenting a rich animal biodiversity and outbreak appears to be periodical. EVD is a conventional zoonotic disease. The evidences indicate that fruit bats are the reservoir for both ebola and Marburg virus. The first indication for the manifestation of Zaire ebola virus in naturally infected fruit bats was recorded by recognition of viral RNA and antibodies in three tree-roosting species: *Hypsignathus monstrosus, Epomops franqueti, Myonycteris torquata* and therefore have been associated as the potential fall over source for ebola virus[17]. Zaire ebola virus has not been well isolated from naturally infected animals. The identification and successful isolation of Marburg virus from the cave-dwelling fruit bat *Rousettus aegyptiacus* provide support to the idea that bats are a reservoir species for filoviruses[19]. Ebola virus might endure as an asymptomatic or subclinical infection in the reservoir species, with little or no transmission and might be intermittently provoked through a suitable stimulus. The stimulus might be stress, co-infection and change in food sources and pregnancy as displayed *in vivo* and *in vitro* investigations[20,21]. This hypothesis describes the infrequent nature and periodicity of EHF in Africa. Mammalian species including NHP vulnerable to infection are considered as the dead end hosts. The probabilities of seasonal outcome on introduction of ebola virus infection have also been proposed[22,23]. The future studies require consideration of the level of infections of ebola viruses in fruit or insectivorous bats in areas prevalent for these viruses. Issues such as virus pathology and perseverance in bats, conceivable activation process of insistent virus and possible transmission routes required to be monitored by field and experimental investigations. Other possible reservoir species and a role for potential augmenting hosts, particularly after the detection of Reston ebola virus in pigs in the Philippines should also be investigated[24].

4. Epidemiology

The first instance of filovirus haemorrhagic fever was reported in 1967 in Germany and the former Yugoslavia and the contributing agent was recognized as Marburg virus[25]. In 1976, epidemic of haemorrhagic fever was reported in two adjacent areas: first in Southern Sudan and consequently in Northern Zaire. The outbreak commenced with malaria like symptoms and transmitted due to application of unsterilized needles in the clinics. An uncertain causative agent was quarantined from patients in both epidemics and named ebola virus after a small ebola river in northwestern Democratic Republic of the Congo. These two outbreaks were caused by two distinct species of ebola virus, Sudan ebola virus (SEBOV) and Zaire ebola virus (ZEBOV)[26-28]. The third African ebola virus species, Tai forest ebola virus (earlier known as Ivory Coast or Cote d'Ivoire) was reported in 1994. The virus was isolated from a diseased ethnologist who had worked in the Tai forest reserve in Cote d'Ivoire and had performed a necropsy on a chimpanzee that had resided with a crowd where numerous members had expired due to EHF[29]. The recent breakthrough is the Bundibugyo ebola virus, existing in equatorial region of Africa[9]. Another ebola virus species, Reston ebola virus (discovered in Reston, Virginia, USA, in November 1989) has been recognized as non-pathogenic for humans[30]. Numerous outbreaks due to several species of ebola virus have been reported in diverse parts of Africa. Historically, EVD has occurred in areas around the rain forests of Central Africa.