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REVIEW OF PAST AND PRESENT EBOLA HEMORRHAGIC FEVER OUTBREAKS IN THE DEMOCRATIC REPUBLIC OF CONGO 1976 -2014

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Abstract

Background: Ebola Hemorrhagic Fever (EHF) has become well known all over the world, especially following the West African outbreak in Guinea, Sierra Leone and Liberia (December 2013). The Ebola virus was first discovered in the Democratic Republic of Congo (DRC), an African country that has continued to register Ebola outbreaks. This study aims to summarize old and new experiences of Ebola in the DRC, in order to propose strategies for better prevention.
Materials and Methods: Information was taken from databases such as PubMed and Cochrane library. A total of eleven full text and three abstracts were identified for the data extraction.
Results: Since its discovery in the DRC, there have been seven Ebola outbreaks, accounting for a total of 1032 cases and 795 deaths. The presence of Non-Human Primates, also considered as the natural reservoir and susceptible host of Ebola virus, can be one major factor that has contributed to the increased number of Ebola outbreaks and cases in the Equatorial region. The existence of rumors and legends related to Ebola in DRC obscure the the viral nature of the disease, and lead to difficulty for health workers, to easily accomplish their tasks.
Conclusion: It is important to scale up community education campaigns designed to give more details on the viral nature of the EHF, establish national agencies and institutions specialized in controlling hunting in the Equatorial region, for better prevention, since there is not yet a specific drug or vaccine to the Ebola Virus.

Key words: Ebola Hemorrhagic Fever; Democratic Republic of Congo; Ebola treatment and prevention

Introduction

Ebola Hemorrhagic Fever (EHF) has become well known and notified disease all over the world, since its last outbreak in Guinea, Sierra Leone and Liberia (December 2013). EHF is caused by the Ebola virus and is responsible for about 50% to 90% death in clinically diagnosed cases (Bonnie L et al., 2005). Efforts to contain this disease have been the focus of the World Health Organization (WHO) and some other countries in recent times. Despite these efforts, no vaccine has yet been licensed for the treatment of the disease.

The Ebola virus was first discovered in the Democratic Republic of Congo (DRC), an African country that has continued to register Ebola outbreaks. The virus was named Ebola following the first outbreak in the town of Yambuku, which is near the Ebola River in Zaire (now the Democratic Republic of Congo); it is at the hospital in this town that the first case of Ebola was identified in September 1976 by the Belgian doctor Peter Piot of the Institute of Tropical Medicine Anvers (Le monde.fr, 1976; Le point.fr, 2014).

This work seeks to provide new insights into these disease outbreaks which have continued to be of a major public health importance in DRC (The case fatality ratio, the strain, the index case and the distribution of the Ebola cases in the country will be discussed), with the ultimate aim of proposing strategies for prevention and early case detection in the DRC.

Etiology

The Ebola virus (EBOV) is the principal etiology of EHF (Paul. et al., 2014). Ebola virus belongs to the family of Filoviridae, to the order of Mononegavirales which includes Rhabdoviridae and Paramyxoviridae. The virion is pleomorphic, producing 'U'-shaped, '6'-shaped, or circular forms but the predominant forms of the virion most frequently seen by electron microscope are long tubular structures. It contains one molecule of linear, single-stranded, negative-sense RNA of 4.2x106 Da (J.J Muyembe et al., 2012).

Ebola hemorrhagic fever (EHF) is caused by any of five genetically distinct members of the Filoviridae family: Zaire ebolavirus (ZEBOV), Sudan ebolavirus (SEBOV), Côte d'Ivoire ebolavirus (CEBOV), Bundibugyo ebolavirus (BEBOV) and Reston ebolavirus (REBOV) (Le Guenno et al., 1995). ZEBOV constitutes a particularly serious threat to both human and Non-Human Primates (NHP) in sub-Saharan Africa. Ebola hemorrhagic fever has been associated with large human outbreaks, with case fatality rates for ZEBOV as high as 90% (Walsh et al., 2003).

Transmission

In most outbreaks, Ebola virus is introduced into human populations via the handling of infected animal carcasses. In these cases, the first source of transmission is an animal found dead or hunted in the forest, followed by person-to person transmission from index case to family members or health-care staff. Animal-to-human transmission occurs when people come into contact with tissues and bodily fluids of infected animals, especially with infected NHPs (Leory et al., 2004).

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The most likely vector of the EBOV is the fruit bat, specifically *Hypsignathus monstrosus* (the hammer-headed fruit bat), Epomops franqueti (Franquet's epaulettes fruit bat), and *Myonycteris torquata* (the little-collared bat) (Leory et al., 2005).The means of transmission within bat populations remains unknown (CDC, 2014).

Human disease is thought to result from consumption of poorly-cooked infected animals, such as bats or chimpanzees (which are known to feed on bats) (Leory et al., 2005; Biek et al., 2006). According to the findings of WHO in October 2014, the most infectious fluids are blood, faeces and vomit. The virus has also been detected in breast milk and urine (OMS, 2014). However unlike other zoonosis, Ebola has the potential of spreading from human to human through exposure of mucous membranes or broken skin to infected body fluids including large aerosol droplets that can be produced during coughing (WHO, 2014).

Clinical features and Diagnosis

The onset of the disease is abrupt after an incubation period of two to 21 days. The clinical features can be divided into four main phases as follows, (1) Phase A. Influenza–like syndrome: The onset is abrupt with non-specific symptoms or signs such as high fever, headache, arthralgia, myalgia, sore throat, and malaise with nausea. (2) Phase B. Acute (day 1–6): Persistent fever not responding to antimalarial drugs or to antibiotics, headache, and intense fatigue, followed by diarrhea and abdominal pain, anorexia and vomiting. (3) Phase C. Pseudo-remission (day 7–8): During this phase the patient feels better and seeks food. The health situation presents with some improvement. Some patients may recover during this phase and survive from the disease and (4) Phase D. Aggravation (day 9): respiratory disorders (dyspnea, throat and chest pain, cough, hiccups), symptoms of hemorrhagic diathesis (bloody diarrhea, hematemesis, conjunctival injection, gingival bleeding, nosebleeds and bleeding at the site of injection consistent with disseminated intravascular coagulation), skin manifestations (petaechiae ,purpura , morbiliform skin rash), neuro-psychiatric manifestations (prostration, delirium, confusion, coma) and cardio-vascular distress and hypovolemic shock (death) (Muyembe et al., 2012).

Patients do not transmit Ebola during the incubation period but become infectious once they develop clinical features of EHF. A diagnosis of EHF can be confirmed by means of several laboratory methods such as an antibody-capture enzyme-linked immunosorbent assay, antigen detection tests, a serum neutralization test, reverse transcriptase polymerase chain reaction (RT-PCR) assay, electron microscopy, or virus isolation by cell culture (WHO. 2014).

From the clinical manifestations it is obvious that EHF may mimic many other tropical diseases like malaria, typhoid fever or yellow fever at the start of the disease. In most outbreaks, recognition of the disease is delayed because physicians are not accustomed to this new illness and the symptoms are generally non-specific. Outside the epidemic context, it appears quite impossible to recognize the first Ebola case in an outbreak on clinical grounds only. Suspicion of EHF is only possible later during the aggravation phase (Muyembe et al., 2012).

Methodology

This study aims to summarize results of publications on Ebola outbreaks in DRC. In order to accomplish this work, information was taken from databases such as PubMed and Cochrane library. Additionally, some articles were taken from google scholar, using the search terms that were utilized for the literature review. This search was focused on past and present Ebola outbreaks in DRC; thus publications without the Ebola outbreak in DRC were not covered within this study. For some abstracts that met the predefined inclusion criteria, full texts were obtained. As of November 2014, a total of eleven full text and three abstracts were qualified for the data extraction.

Ebola outbreaks in DRC

Table 1 illustrates that, since the discovery and the first reported case of Ebola in the DRC, there have been seven Ebola outbreaks, accounting for a total of 1032 cases and 795 deaths. Three of the outbreaks occurred in the Equator province; six were attributed to ZEBOV strain while only one is attributed to the BEBOV strain.

Table 1: Description of Ebola outbreaks in DRC (From1976 outbreak to 2014 outbreak)

Outbreak year	Index, localization and Characteristics of the outbreak
1976 (ZEBOV)	Occurred In Yambuku, the index case was a 44 year-old male, who felt ill after eating fresh and smoked antelope and monkey. 318 cases were recorded, with a case fatality rate (CFR) of 88% (WHO, 1979)
1977(ZEBOV)	Noted retrospectively in the village of Tandala. One person was reported, and died. CFR is 100% (Heymann et al.,1980) .
1995 (ZEBOV)	The index case was farming and preparing charcoal in the remnant forest areas of Kikwit, there were also a lot of bats and rodents in the region, (Guimard et al.,1995).315 cases(250 deaths), CFR of 81% (Khan et al., 1999).
2007(ZEBOV)	In Mweka, West Kasai Province. The index case was the chief of the village and a hunter. 264 cases (187deaths), CFR of 71%.Associated with a massive fruit bat migration through this region (Leory et al., 2009).
Dec 2008 to Feb 2009 (ZEBOV)	In the Mweka and Luebo health zones of the west Kasai Province. The index case was believed to be an 18 year old girl, 32 cases (15 deaths) were reported, with a CFR of 47% (Muyembe et al., 2012).
2012 (BEBOV)	In Isiro and Dungu, Province Orientale (Albarino et al., 2002). 36 cases (13 deaths) were reported, CFR of 36 % Caused by BEBOV strain (CDC, 2014).
2014 (ZEBOV)	In Equator province, the index patient was a pregnant woman living in Inkanamongo village, who butchered a monkey (Gael et al., 2014). 66 cases (49deaths) were reported, CRF of 74 %(CDC, 2014) .

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Distribution of Ebola registered cases in DRC

Figure 1 shows that Equator province registered more cases of Ebola (37.30%) than any other provinces.
The Equator province, as well as the other provinces, which have registered Ebola cases have a common characteristic: they form a part of the large equatorial forest. Mostly, many types of NHPs are found in equatorial forest. It is likely that the presence of these NHPs, which are also considered to be the natural reservoir and susceptible host of Ebola virus, may be one of major factors that has contributed to the increased number of Ebola outbreaks and cases in this region.

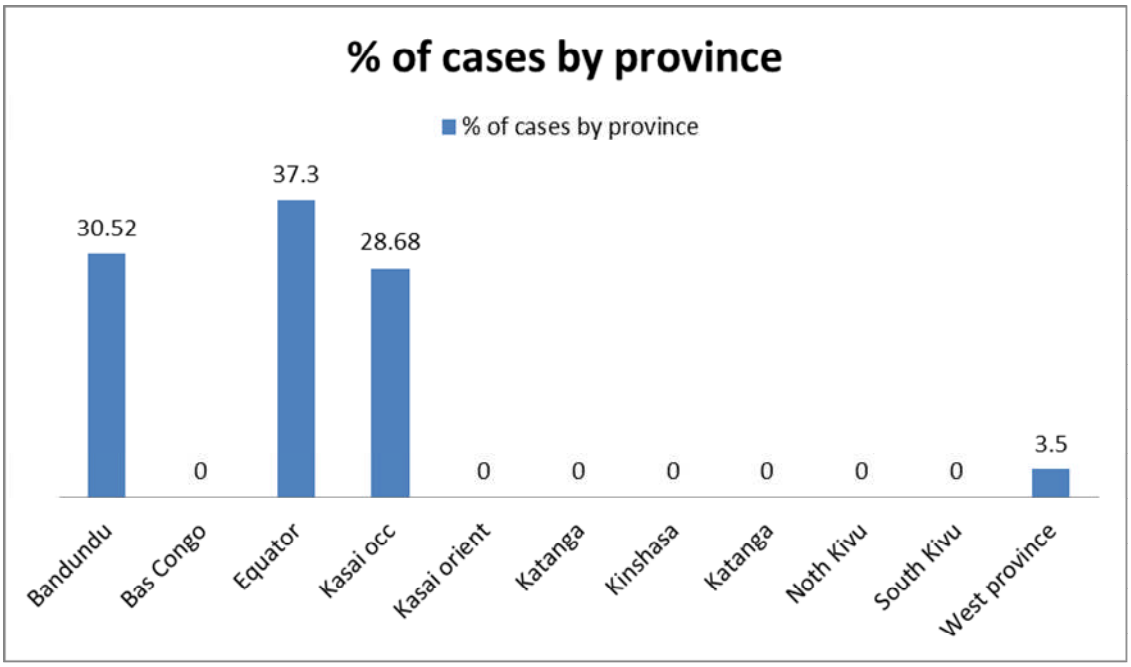

Figure 1: Percentage of registered cases by province

It has been shown that tropical rain forests of Africa to which the Western Congo Swamp Forests near Yambuku, Taï Forest in Côte d'Ivoire and Minkebé Forest in Gabon belong constitute a common ecosystem for Ebola virus emergence providing rich animal biodiversity and as such epidemics appear to be seasonal. Documented human and non-human EHF outbreaks occurred mainly during wet seasons, marked by fruit abundance. The index case of the 1995 EHF outbreak in Kikwit fell ill in January and the 1994 EHF outbreak amongst chimpanzees in the Tai forest occurred in November, at the end of the wet season (Muyembe et al., 2012).

Also the equatorial forest is a poorly developed region, where the population lives essentially by hunting. It is important to note that Ebola outbreaks in DRC tend to occur more in a rural areas than urban areas. The last outbreak of Ebola in DRC (August to November 2014) also occurred in rural area, while the west Africa outbreak marks the first outbreak in a densely populated urban area within Conakry's large shanty towns (Diallo, 2014).

Ebola Virus in health care professionals

The major difference between the management of the Ebola epidemic and others, such as the HIV epidemic, is that the Ebola virus present a more challenging health hazard to health care providers. Nurses, doctors, Red Cross volunteers, and other health care workers stand the risk of being infected with the Ebola virus while providing care. The risk of EHF contamination among these health care professionals is also increased in a continent like Africa where the nurses and other health care providers work under extraordinarily difficult conditions, lacking such basic infection control tools as bleach, soap, and gloves (Bonnie et al., 2005).

When an Ebola patient, comes with non-diagnosed EHF in a hospital, the chain of contamination can start with the health care provider that offers the first care. This was the case, a local doctor and three health workers, who undertook a postmortem cesarean section on the index case of the 2014 outbreak. Both were not only infected and died; but became the evident source of further transmission in this outbreak (Gael et al., 2014). Deaths caused by EHF among health care professional has been very remarkable. The 1995 Democratic Republic of the Congo (DRC) outbreak devastated health care workers, Out of the 250 individuals who died, 47 (approximately 20%) were health care professionals (Guimard et al., 1995). In the last outbreak, from the 49 registered deaths, 8 were health care professionals (Gael et al., 2014).

The existence of rumors and legends related to the outbreaks could obscure the viral nature of the disease (Muyembe et al., 2012), and this can lead to difficulty, for health workers, to easily accomplish their tasks.

In Kikwit (DRC), anyone associated with Ebola was likely to have experienced stigmatization. At a point during the outbreak, local people thought Ebola originated with the medical staff working in the hospital. All those who had died had been in a hospital. Therefore, the people reasoned that, it was the health care workers who were killing people. This rumor demoralized the local health care workers and made it difficult for nurses at home and in the community. The nurses and doctors had to deal with not only a panicked and fearful public, essentially absent public health and medical resources, but also they themselves were seen as agents of death (Bonnie et al., 2005).

Treatment

There is no effective drug and specific vaccine for EHF. Only supportive care could be administered, to sustain cardiac and renal functions with prudent use of perfusion. Oral rehydration can be recommended but sometimes not realistic because of throat pain, vomiting and intense fatigue (Muyembe et al., 2012). In a clinical experiment conducted late in the 1995 Ebola outbreak in Kikwit, human convalescent blood was used for passive immunization to treat patients that had been infected naturally with ZEBOV; seven out of eight patients, who received blood transfusion from convalescent Ebola patients survived (Mupapa et al., 1999). Such experiments, unfortunately, have not been repeated in further outbreaks because *in vitro* studies showed that antibodies against Ebola had no neutralizing activities. In addition, although monoclonal antibodies to the glycoprotein of Ebola virus showed protective and therapeutic properties in mice, they failed to protect NHP (Gupta et al., 2001; Oswald et al., 2007). The development of a vaccine against Ebola has been hindered by the lack of interest and investment by pharmaceutical companies in researching an infection with a previously very low disease burden confined to poor developing countries. Dr Anthony Fauci, director of America's National Institute of Allergy and Infectious Diseases (NIAID) recently announced that phase I clinical trials of a promising Ebola vaccine are to be initiated in September 2014, hoping for favorable results by January and very optimistically to have this vaccine manufactured and available for distribution by late 2015 (Paul et al., 2014).

Control measures

Many countries all over the world have put public health measures in place to control EHF. These measures include checking and screening for EBOV at the airports and other points of entry, quarantine of people coming from regions associated with Ebola, and isolation of suspected and clinically diagnosed patients. The corner-stone for controlling an outbreak of EHF is to interrupt the viral transmission chain (Muyembe et al., 2012). In the DRC, most of the time; outbreaks are managed by the Congolese health ministry, and WHO. Their activities include field investigations, disease surveillance, infection control, clinical management, social mobilization and community health education (WHO, 2007).

Conclusion

Ebola hemorrhagic fever continues to be a public health problem in the DRC. Since its discovery in the DRC, Ebola outbreaks have occurred more than seven times, tend to occur more in Equator region and have caused 795 deaths. It is important to put in place strategies for better prevention, at present there is no specific drug or vaccine for the treatment and prevention. The burden of preventing and controlling this disease therefore rests on the Public health authorities of the DRC and their partners to work towards: Increase awareness through health education of the population through campaigns about EHF with particular attention to: hygienic measures, cooking of bush meat as long as possible, avoiding coming into contact with the biological fluids from persons suspected or diagnosed with a hemorrhagic fever. Organizing community education campaigns designed to give more details on the viral nature of the EHF, in order to reduce rumors and false beliefs about the disease. Establishing national agencies and institutions specialized in controlling hunting in the Equator region, in order to avoid the consumption of infected animals. Expanding training of qualified people for better management of the outbreak, and increase supply of medical materials to isolated rural areas. Establishing structures in every health zone of the country, for early detection of any future outbreaks. Motivating the health care professionals, especially those working in the zone with previous Ebola outbreaks.

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