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CLINICAL ASPECTS OF EBOLA HEMORRHAGIC FEVER: A REVIEW

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ABSTRACT

Ebola hemorrhagic fever is a viral disease marked by fever, systemic hemorrhage, and high mortality; it affects humans and monkeys and has appeared in epidemic form in Africa and Germany. The cause is one of the three subtypes of viruses in the Filoviridae family that is distinguished by long thread like strands of RNA. The animal or insect host (reservoir) has not been identified, limiting study of the disease. The three filoviruses known to cause disease in humans are the Marburg virus, Zaire virus, and Sudan virus. The fourth subtype, the Reston virus, is fatal to monkeys, but did not produce disease in infected**.** In the present article, we have concentrated on clinical features, diagnosis, transmission, prevention and treatment of Ebola hemorrhagic fever. The aim of present article is to provide in depth knowledge about the clinical aspects of Ebola hemorrhagic fever.

KEYWORDS

Ebola hemorrhagic fever, Ebola Virus, Filovirus and Viral hemorrhagic fever.

INTRODUCTON

Ebola hemorrhagic fever (EHF) is a severe, often-fatal disease in humans and nonhuman primates (monkeys, gorillas, and chimpanzees) that has appeared sporadically since its initial recognition in 1976. The disease is caused by infection with Ebola virus, named after a river in the Democratic Republic of the Congo (formerly Zaire) in Africa, where it was first recognized. The virus is one of two members of a family of RNA viruses called the Filoviridae. There are four identified subtypes of Ebola virus. Three of the four have caused disease in humans: Ebola-Zaire, Ebola-Sudan, and Ebola-Ivory Coast. The fourth, Ebola-Reston, has caused disease in nonhuman primates, but not in humans[1]. EHF typically appears in sporadic outbreaks coinciding with the rainy season, and is usually spread in humans within a health-care setting[2].

DESCRIPTION ABOUT EBOLA VIRUS

Ebola is the virus EBOLA VIRUS (EBOV), a viral genus, and the disease Ebola hemorrhagic fever (EHF), a viral hemorrhagic fever (VHF). The virus is named after the Ebola River Valley in the Democratic Republic of the Congo (formerly Zaire), which is near the site of the first recognized outbreak, a mission hospital run by

Flemish nuns, in 1976[3]. There are four recognized species within the Ebola virus genus, which have a number of specific strains[4]. Electron micrographs show long filaments, characteristic of the Filoviridae viral family. The virus interferes with the endothelial cells lining the interior surface of blood vessels and with coagulation. As the blood vessel walls become damaged and the platelets are unable to coagulate, patients succumb to hypovolemic shock. Ebola is transmitted through bodily fluids, while conjunctiva exposure may also lead to transmission. However, it remained largely obscure until 1989 when several widely publicized outbreaks among monkeys in the United States occurred[5]. The different types of Ebola virus are-:

- **Zaire virus (ZEBOV):** It has the highest case-fatality rate, up to 90% in some epidemics. The first outbreak took place on 26 August 1976 in Yambuku. Mabalo Lokela, a 44-year-old schoolteacher, became the first recorded case. The symptoms resembled malaria, and subsequent patients received quinine. The initial transmission was believed to be due to reuse of the needle for Lokela's injection without sterilization. Subsequent transmission was also due to lack of barrier nursing and the traditional burial preparation method, which involves washing and gastrointestinal tract cleansing[6].
- **Sudan Ebola virus (SEBOV):** The virus was the second species of Ebola emerging simultaneous with the Zaire virus. It was believed to have originated amongst cotton factory workers in Nzara, Sudan, with the first case reported as a worker exposed to a potential natural reservoir. The carrier is still unknown. The most recent outbreak occurred in May 2004. 20 confirmed cases were reported in Yambio County, Sudan, with five deaths resulting. The average fatality rates for were 54% in 1976, 68% in 1979, and 53% in 2000 and 2001[7].
- **Cote d'Ivoire Ebola virus (CIEBOV):** It is also referred to as Ivory Coast ebolavirus and Tai Ebola virus; it was first discovered among chimpanzees from the Tai Forest in Côte d'Ivoire, Africa. Studies of tissues taken from the chimpanzees showed results similar to human cases during the 1976 Ebola outbreaks in Zaire and Sudan. As more dead chimpanzees were discovered, with many testing positive to Ebola using molecular techniques. 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 Ebola. She developed symptoms similar to those of dengue fever approximately a week after the necropsy, and was transported to Switzerland for treatment. She was discharged from hospital after two weeks and had fully recovered six weeks after the infection.
- **Reston Ebola virus (REBOV):** Discovered during an outbreak of Simian hemorrhagic fever virus (SHFV) in crab-eating macaques from Hazleton Laboratories (now Covance) in 1989. Since the initial outbreak in Reston, Virginia, it has emerged in the Philippines, Siena Italy, and Texas. It is non-pathogenic to humans however hazardous in monkeys[8].

SIGN AND SYMPTOMS OF EBOLA HEMORRHAGIC FEVER

The incubation period ranges from 2 to 21 days, with an average of 5 to 10 days, fever, myalgia, and headache begin abruptly, followed by some combination of nausea, vomiting, diarrhoea, abdominal pain, impaired kidney, rash, sore throat, cough, pharyngitis, conjunctivitis, lymphadenopathy, and jaundice. Petechiae and bleeding from mucous membranes and injection sites then appear. Central nervous system involvement is indicated by delirium and a decreased level of consciousness. A maculopapular rash on the trunk usually develops around day 5.

By the day 10, the fever disappears, and patients either improve or die from irreversible hemorrhage and necrosis of the liver and other major organs. Severe organ necrosis marks the terminal stage. Mortality has ranged from 25% during the Marburg epidemic to approx. 60% for the Sudan virus and 90% during the Zaire epidemics[9].

DIAGNOSIS

Methods of diagnosis of Ebola include testing saliva and urine samples. Ebola is diagnosed with an Enzyme-Linked ImmunoSorbent Assay (ELISA) test. This diagnosis method has produced potentially ambiguous results during non-outbreak situations. To combat the false positives, a more complex test based on the ELISA system was developed by Tom Kzaisek at USAMRIID, which was later improved with Immunofluorescent antibody analysis (IFA). It was however not used during the serosurvey following Reston. These tests are not commercially available[10].

PREVENTION

In the early stages, Ebola may not be highly contagious. Contact with someone in early stages may not even transmit the disease. As the illness progresses, bodily fluids from diarrhea, vomiting, and bleeding represent a hazard. Due to lack of proper equipment and hygienic practices, large-scale epidemics occur mostly in poor, isolated areas without modern hospitals or well-educated medical staff[11]. Many areas where the infectious reservoir exists have just these characteristics. In such environments, all that can be done is to immediately cease all needle-sharing or use without adequate sterilization procedures, isolate patients, and observe strict barrier nursing procedures with the use of a medical rated disposable face mask, gloves, goggles, and a gown at all times. This should be strictly enforced for all medical personnel and visitor. Vaccines have successfully protected non-human primates, however the six months needed to complete immunization made it impractical in an epidemic[12].

TREATMENT

There is no standard treatment for Ebola hemorrhagic fever. Treatment is primarily supportive and includes minimizing invasive procedures, balancing electrolytes, and, since patients are frequently dehydrated, replacing lost coagulation factors to help stop bleeding, maintaining oxygen and blood levels, and treating any complicating infections[13].

Convalescent plasma (factors from those that have survived Ebola infection) shows promise as a treatment for the disease. In monkeys, administration of an inhibitor of coagulation (rNAPc2) has shown some benefit, protecting 33% of infected animals from a usually 100% (for monkeys) lethal infection. Development of improved Morpholino antisense drug conjugated with cell penetrating peptides is ongoing[14].

PROGNOSIS:

Ebola hemorrhagic fever is potentially lethal and encompasses a range of symptoms including fever, vomiting, diarrhea, generalized pain or malaise, and sometimes internal and external bleeding. The span of time from onset of symptoms to death is usually between 2 and 21 days[15]. By the second week of infection, patients will either defervesce (the fever will lessen) or undergo systemic multi-organ failure. Mortality rates are typically high, with the human case-fatality rate ranging from 50–89%, depending on the species or viral strain. The cause of death is usually due to hypovolemic shock or organ failure[16]. The table 1 shows statistical data of Ebola hemorrhagic fever of different countries.

MODES OF TRANSMISSION

- The Ebola virus is transmitted by direct contact with the blood, secretions, organs or other body fluids of infected persons.
- Burial ceremonies where mourners have direct contact with the body of the deceased person can play a significant role in the transmission of Ebola.
- The infection of human cases with Ebola virus through the handling of infected chimpanzees, gorillas, and forest antelopes -- both dead and alive -- has been documented in Côte d'Ivoire, the Republic of Congo and Gabon. The transmission of the Ebola Reston strain through the handling of cynomolgus monkeys has also been reported[17].
- Health care workers have frequently been infected while treating Ebola patients, through close contact without correct

infection control precautions and adequate barrier nursing procedures.

- The virus has been confirmed to be transmitted through body fluids. Transmission through oral exposure and through conjunctiva exposure is likely, which have been confirmed in non-human primates[18].
- Filoviruses are not naturally transmitted by aerosol. They are, however, highly infectious as breathable 0.8-1.2 micron droplets in laboratory conditions.

CONTAINMENT

- Suspected cases should be isolated from other patients and strict barrier nursing techniques implemented.
- Tracing and following up people who may have been exposed to Ebola through close contact with patients are essential.
- All hospital staff should be briefed on the nature of the disease and its transmission routes. Particular emphasis should be placed on ensuring that invasive procedures such as the placing of intravenous lines and the handling of blood, secretions, catheters and suction devices are carried out under strict barrier nursing conditions. Hospital staff should have individual gowns, gloves, masks and goggles. Non-disposable protective equipment must not be reused unless they have been properly disinfected[19].
- Infection may also spread through contact with the soiled clothing or bed linens from a patient with Ebola. Disinfection is therefore required before handling these items.
- Communities affected by Ebola should make efforts to ensure that the population is well informed, both about the nature of the disease itself and about necessary outbreak containment measures, including burial of the deceased. People who have died from Ebola should be promptly and safely buried[19].

Table 1

Ebola Hemorrhagic Fever: Statistics of Different Countries

Year(s)	Country	Ebola Subtype	Reported no. of human cases	Reportd no. (%) of deaths among cases	Situation
1967	Zaire[Democratic Republic of Congo(DRC)]	Ebola-Zaire	318	280	Occurred in Yambuku and Surrounding area. Disease was spread by close personal contact and by use of contaminated needles and syringes in hospitals/clinics. This outbreak was the first recognition of the disease[20].
1976	Sudan	Ebola-Sudan	284	151	Occurred in Nzara, Maridi and the surrounding area. Disease was spread mainly through close personal contact within hospitals. Many medical care personnel were infected[21].
1976	England	Ebola-Sudan	1	0	Laboratory infection by accidental stick of contaminated needle[22].
1977	Zaire	Ebola-Zaire	1	1	Noted retrospectively in the village of Tandala[23].
1979	Sudan	Ebola-Sudan	34	22	Occurred in Nzara, Maridi. Recurrent outbreak at the same site as the 1976 Sudan epidemic[24].
1989	USA	Ebola-Reston	0	0	Ebola-Reston virus was introduced into quarantine facilities in Virginia,

					Texas, and Pennsylvania by monkeys imported from the Philippines[25].
1990	USA	Ebola-Reston	4 (asymptomatic)	0	Ebola-Reston virus was introduced once again into quarantine facilities in Virginia, and Texas by monkeys imported from the Philippines. Four humans developed antibodies but did not get sick[26].
1989-1990	Philippines	Ebola-Reston	3 (asymptomatic)	0	High mortality among cynomolgus macaques in a primate facility responsible for exporting animals in the USA[27]. Three workers in the animal facility developed antibodies but did not get sick[28].
1992	Italy	Ebola-Reston	0	0	Ebola-Reston virus was introduced into quarantine facilities in Sienna by monkeys imported from the same export facility in the Philippines that was involved in the episodes in the United States. No humans were infected[29].
1994	Gabon	Ebola-Zaire	52	31	Occurred in Mékouka and other gold-mining camps deep in the rain forest. Initially thought to be yellow fever; identified as Ebola hemorrhagic fever in 1995[30].
1994	Ivory Coast	Ebola-Ivory Coast	1	0	Scientists became ill after conducting an autopsy on a wild chimpanzee in the Tai Forest. The patient was treated in Switzerland[31].
1995	Democratic Republic of the Congo (formerly Zaire)	Ebola-Zaire	315	250	Occurred in Kikwit and Surrounding area. Traced to index case-patient who worked in the forest adjoining the city. Epidemic spread through families and hospitals[32].
1996	Gabon	Ebola-Zaire	37	21	Occurred in Mayibout area. A chimpanzee found dead in the forest was eaten by people hunting for food. Nineteen people who were involved in the butchery of the animal became ill;other cases occurred in family members[30].
1996-1997	Gabon	Ebola-Zaire	60	45	Occurred in Booué area with transport of patients to Libreville. Index case- patient was a hunter who lived in a forest camp.Disease was spread close contact with infected persons. A dead chimpanzee found in the forest at the time was

					determined to be infected[30].
1996	South Africa	Ebola-Zaire	2	1	A medical professional traveled from Gabon to Johannesburg, South Africa, after having treated Ebola virus-infected patients and thus having been exposed to the virus. He was hospitalized, and a nurse who took care of him became infected and died[33].
1996	USA	Ebola-Reston	0	0	Ebola-Reston virus was introduced into a quarantine facility in Texas by monkeys imported from the Philippines. No human infections were identified[34].
1996	Philippines	Ebola-Reston	0	0	Ebola-Reston virus was identified in a monkey export facility in the Philippines. No human infections were dentified; one animal handler has bola antibody[35].
2000-2001	Uganda	Ebola-Sudan	425	224	Occurred in Gulu, Masindi,and Mbarara districts of Uganda. The three most important risks associated with Ebola virus infection were attending funerals of Ebola hemorrhagic fever case-patients, having contact with case-patients in one's family, and providing medical care to Ebola case-patients without using adequate personal protective measures[36].
2001-2002	Gabon	Ebola-Zaire	65	53	Outbreak occurred over the order of Gabon and the Republic of the Congo[37].
2001-2002	Republic of Congo	Ebola-Zaire	57	43	Outbreak occurred over the border of Gabon and the Republic of the Congo.This was the first time that Ebola hemorrhagic fever was reported in the Republic of the Congo[37].
2002-2003	Republic of Congo	Ebola-Zaire	143	129	Outbreak occurred in the districts of Mbomo and Kéllé in Cuvette Ouest Département[38].
2003	Republic of Congo	Ebola-Zaire	35	29	Outbreak occurred in Mbomo and Mbandza villages located in Mbomo district,

					Cuvette Ouest Département[39].
2004	Sudan	Ebola-Sudan	17	7	Outbreak Occurred inYambio county of southern Sudan. This outbreak was concurrent with an outbreak of measles in the samearea, and several suspected EHF cases were later reclassified as measles cases[40].
2007	Democratic Republic of Congo	Ebola-Zaire	264	187	Outbreak occurred in Kasai Occidental Province.The outbreak was declared over November 20. Last confirmed case on October 4 and last death October 10[41].
2008	Philippines	Ebola-Reston	6	0	First known occurrence of Ebola-Reston in pigs. Strain closely similar to earlier strains. Six workers from the pig farm and slaughterhouse developed antibodies but did not become sick[42, 43].

CONCLUSION:

It may be concluded that Ebola hemorrhagic fever is a rare viral disease that causes severe bleeding and results in death in up to 90 percent of those infected. The Ebola virus is transmitted by direct contact with the blood, body fluids and tissues of infected persons. Transmission of the Ebola virus has also occurred by handling sick or dead infected wild animals (chimpanzees, gorillas, monkeys, forest antelope, fruit bats). The review is aimed at Ebola hemorrhagic fever, its sign, symptoms, diagnosis, mode of transmission, prognosis as well as treatment. The complaint of Ebola hemorrhagic fever s is common but presents a challenging diagnostic exercise. Attempt is made in above review article to enumerate various clinical aspects of Ebola hemorrhagic fever. More vaccines should be discovered which would be beneficial in the treatment of Ebola hemorrhagic fever.

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