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REVIEW ARTICLE OPEN ACCESS

EBOLA VIRUS: A BRIEF ARTICLE

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ABSTRACT:

The disease caused by Ebola virus infection is one of the most fatal disorders known to mankind because of its higher mortality rate (up to 85%) accompanying the disease. Animals also suffer from Ebola hemorrhagic fever (EHF) infectious, it can be transmitted to both human and non-human primates. The first epidemic of EHF occurred in 1976 with the incubation period is less than 21 days in Zaire, Africa (now Democratic Republic of Congo). Filoviridae family classified into five genetically distinct members who are responsible for EHF are as follows: Sudan, Côte d'Ivoire, Zaire, Reston, and Bundibugyo ebolavirus. The Ebola epidemic in 2014 is the largest ever reported disease in history, affecting multiple countries in West Africa and being imported to other countries. The natural host of Ebola is not known, thus it is not possible to carry out certain trials to regulate or prevent viruses from transmission to people. At present, there is no drug or vaccine which is helpful against ebolavirus infection in humans and non-humans. Certain precautionary measures have to taken to avoid transmissions of the Ebola Virus.

KEYWORDS: Ebola Virus, Filoviridae, EVD, EHF.

INTRODUCTION:

The Ebola virus causes infections related to Ebola virus, in humans beings and non-human primates.[1]Ebola virus diseases (EVDs) discovered in 1976 by Dr. Peter Piotin in Zaire, Africa (now it is popularly known as the Democratic Republic of Congo or DR Congo) from the blood of a woman who is a catholic nun who suspected of having yellow fever.[2]The disease is zoonotic, and proof suggests the involvement of fruit bats as the main reservoir.[3] It originates from the genus Ebola with family Filoviridae, according to "The International Committee on Taxonomy of Viruses" (ICTV).[4] No Ebola Virus Disease outbreaks were reported between the year 1979 to 1994, but after 1994 the number increased, leading to the discovery of two new Ebolavirus species (BDBV and TAFV).[5] In 1989, another Ebola Virus species was discovered known as Reston Ebola virus in the United State of America during an outbreak of viral haemorrhagic fever among crab-eating macaque also called as long-tailed macaque which wasimported from island of the Philippines and was found to be non-pathogenic in humans.[6]The 2014 Ebola epidemic is one of the largest ever reported EVD in history, affecting multiple countries in West Africa and being imported to several other countries: one severe infection case was reported in Spain while one death occurs in the United States and two locally acquired cases in healthcare were reported.[7] Since the start of the biggest flare-up of Ebola contamination in Guinea found in December 2013, and up to 6 January 2016, there have been 28,637 affirmed, and suspected EVD cases, bringing about 11,315 passings (39.5%). The most influenced nations, Guinea, Sierra Leone, and Liberia, interfered with the human-to-human transmission and were announced No Ebola infection on 7 November 2015, 29 December 2015, and 14 January 2016, respectively. They are all in a 90-day time of increased observation. There have been 881 affirmed

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instances of EVD among wellbeing laborers, with 513 announced passings. [8] The present review is an attempt to summarize various essential aspects of EVD.

VIROLOGY:

EBOV is a zoonotic filovirus, comprised of envelope, nonsegmented negative-stranded RNA. Mononegavirales belonging to the Filoviridae family, is composed of three genera, Ebolavirus,Cuevavirus and Marburgvirus.[9] To date five species of Ebolavirus have been identified: Zaire ebolavirus, Bundibugyo ebolavirus, Tai Forest ebolavirus (formerly known as Cote d'Ivore), Sudan ebolavirus, and Reston ebolavirus (found in Western Pacific, highly pathogenic in nonhuman primates).[10] The Ebola virus genome is 19 kb long, with seven open reading frames encoding structural proteins, including the virion envelope Proteins which are associated with nucleic acid also called as nucleoprotein (NP), Proteins which are associated with carbohydrates also called as glycoprotein (GP), and matrix proteins VP24 and VP40; nonstructural proteins, including VP30 and VP35; and the viral polymerase. Just like that of Marburg virus, the Glycoprotein open reading frame of the Ebola virus gives rise to two gene products, a soluble full-length 150- to 170-kDa protein (GP) and a60- to 70-kDa protein (sGP) that inserts into the viral membrane, through transcriptional editing.[11]

ECOLOGY:

In connection with an acute outbreak, The epidemic provided an opportunity to search for the elusive reservoir of the Ebola virus. It is not widely appreciated that there is only one reported study of any search for the reservoir.[12] The first convincing evidence for a reservoir was detected as both nucleic acids and antibodies in several bats species, although isolation of virus from these species remains to be demonstrated as conclusive evidence of infection. Also, this observation fits with several historical observations linking EBOV outbreaks to seasonal patterns and mining and cave exploration.[13] Filoviruses get circulate widely in the central African rain forests and where they infect humans as well as nonhuman primates, such as baboons and mandrills. and also, in gorillas and chimps. The data in the Leroy et al. article show that the virus has been circulating in these regions. It was claimed that Ebola is not necessarily lethal in the primates, but the strain and the virulence of infecting the Ebola virus remain unclear. We have an idea of the original Marburg virus outbreak that filoviruses could infect primates because Marburg virus was first discovered in infected monkeys of Circopithecus aethiops species that are shipped from Uganda.[14] Ebolavirus are circulated across several distinct mammal clades, such as Old World fruit bats, primates, and artiodactyls.[15] A broad-based One Health approach incorporating these ecological concepts in the control of Ebola Virus Disease can effectively improve or prevent an infection now and in the future.[16]

EPIDEMIOLOGY:

Ebola virus disease is a zoonotic disease and each flare-up in the human population is start off by an introduction from an animal reservoir (e.g. due to hunting, direct contact with infected live or dead animals, consuming of bush meat). The spread of sporadic cases appearing among the rural population living near the rainforest, to the large urban agglomerations is responsible for the development of a new epidemic.[17] During the ninth Ebola Virus Diseaseflare-up in the first 2018 semester in E´ quateur Province in DRC, there was a total of 54 cases with 33 deaths (case fatality ratio [CFR], 61%). A vaccination treatment was successfully applied to patients between May and June 2018, with a total of 3481 people vaccinated, The vaccination treatment was first given to frontline health care workers on priority categories, and EVD primary and secondary contacts. Later, on 01 August 2018, the Democratic Republic of Congo Ministry of Health declared an outbreak of

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EBOV in the North Kivu province, this is the country's 10th outbreak after its discovery in 1976. Since then, the EBOV epidemic has circulated in the Ituri provinces. As of 28 March 2019, a total of 1044 cases (978 confirmed and 66 may positive cases) and 652 deaths (586 confirmed and 66 likely) have been reported.[18] As of late, a medical attendant got tainted with Ebola infection in Spain in the wake of offering treatment to a contaminated person. Extra individuals may have likewise been optionally influenced. Lack of knowledge in the use of personal protective equipment (PPE) and absence of a regulation arrangement and introduction follow-up appear to have happened.19] Once introduced into the population EBOV may spread rapidly, due to the rapid uncontrolled rate of high levels of virus replication and virus shedding in body fluids (saliva, urine, faeces, and sweat) by EVD patients.[20] At the point when cleanliness and individual defensive measures are not sufficient, the risk for infection of healthcare workers is considerable, Furthermore cultural aspects, for example, neighbourhood memorial service functions with potential contact with body liquids from patients who have died by Ebola Infection, add to the greatness of this flare-up.[21-22]

PATHOPHYSIOLOGY:

Ebola virus (EBOV) is present in the form of a thread or filament covered with the membrane structure contains a negative-strand RNA genome which is 19 kb in length and encodes for a protein which is bounded with nucleic acid called as nucleoprotein (NP), glycoprotein (GP), RNA-dependent RNA polymerase (L), and four structural proteins termed VP24, VP30, VP35, and VP40.[23] Viral replication is carried out by NP, VP35, and L; the active polymerase complex is composed of VP35 (a polymerase cofactor) and L (polymerase) while NP drives RNA encapsidation.[24] VP30 is a transcriptional activator and is also involved in nucleocapsid formation and assembly. One of the matrix protein VP24, contributes to nucleocapsid formation whereas VP40 matrix protein ease the budding of progeny virion from infected cells. One of the major task is to covers the surface of the virion is done by Protein bound to carbohydrates called Glycoprotein (GP) and is the sole host attachment factor for Ebola Virus. Moreover, Ebola Virus expresses two soluble forms of Glycoprotein, secreted glycoprotein, and Small soluble Glycoprotein through RNA editing.[25]

TRANSMISSION:

Forty years later the first recorded flare-up of Ebola virus infection, the specific method of transmission and the natural reservoir of the virus are still discussed. Bigger mammals such as gorillas also become sick and give up to the Ebola infection sickness. This demonstrated before that they are, similar to people, which are the traditional end has instead of an essential store animal categories, with distinct repository species not displaying infection side effects by definition. Early it was very difficult to identify the natural animal reservoir of Ebolavirus have been challenged by Africa's vast biodiversity. From the vast list of categories of possible reservoir hosts, fruit bat species was identified as possible reservoir hosts.[26] Transmission occurs by maintaining close contact with body liquids of contaminated patients. The hatching time of Ebola Virus Disease is ofnormal 5-9 days, with a sclae of 1-21 days in 95% or greater amount of patients, and patients are not considered contaminated by the disease until they develop symptoms of virus.[27-28] Ebola virus disease is not generally considered an airborne infection but rather is primarily transmitted among humans by contact with infected bodily fluids or contaminated objects.[29]The virus may remain in semen andmaternal milk even after complete treatment from the disease, and there are documentary evidence of transmission of disease to family members or those who come in contact with the patient who successfully recovered from EVD. There is no full proofconfirmation that objects or materials which are likely to carry infection, such as clothes, utensils, and furniture can spread the disease, however, caution is taken. The virus is found to be sensitive to UV radiation, but 3 to 10% of viable viruses were found in the only study that tested dried inoculums. Although the disease is not taken into consideration eitherborne in water or food.[30] Ebolavirus rarely spreads through the respiratory

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route. Of interest, the persistence of the Ebola viral RNA in convalescing individuals has been reported, likely due to replicating intracellular nucleocapsids.[31] This virus has the capability to survive at any place in the globe with no time through modern transportation. The investigation suggested that ecological elements are likewise connected with the transmission of Ebola infection disease particularly to the humid conditions and may enhance spread of virus from its cryptic reservoir to humans.[32]

SYMPTOMS:

The hatching time is between 5-9 days, with a scale from 1-21 days. A range of clinical manifestations of EVD occur, from mild to the rapidly fulminant. Early signs and symptoms of Ebola Virus Disease may be like to other causes of fever, such as malaria, dengue, Lassa fever, Marburg, Crimean Congo hemorrhagic fever, typhoid, shigellosis, rickettsial diseases, borreliosis, leptospirosis, and viral hepatitis.[33] Gastrointestinal symptoms such as watery diarrhea, nausea, vomiting, or abdominal pain typically follow. Other symptoms and signs including Paining in Chest, headache, conjunctival injection, dyspnea, confusion, and bleeding may occur. The virus enters the reservoir host through skin or mucosal surfaces; invades the macrophages, monocytes, and dendritic cells; replicates; and then disseminates via lymphatic and hematogenous routes. The characteristic hemorrhagic nature of Ebola Virus Disease is because of the release of cytokines that cause endothelial leakage, vascular instability, and coagulation abnormalities. The end result of the disease process mimics septic shock with impaired host immune response, hypotension, and multi-organ failure.[34] Children also shows the similar symptoms to adults; however, kids are reported to have more respiratory and GIT symptoms, but less loss of blood and neural signs, as compare to adults. Generally, children under 4 years age difficult to identify the disease, before affected with a fever and often diagnosis is late. In severe infection large number organ dysfunction is common and includes acute kidney injury, adrenal failure, pancreatitis, and damage to liver. Hepatitis is common, with higher concentration of aspartate aminotransferase than alanine aminotransferase, although jaundice is not majorly seen. Renal dysfunction is also a common symptom in severe cause of disease but can be treatedby maximum concentration of liquid intake in the primary stages. In first step of the disease it may be caused by loss of water from body, but in most severe stages it damage to the kidneys by the Ebola virus. Massive bleeding, typically in the GIT (for example, diarrhoea with blood), is usually seen only in rare cases. Internal bleeding may not seen if there are no external signs of the bleeding inside of the body is observed.[35-37]

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Fig 1: Early signs and symptoms of Ebola virus

DIAGNOSIS:

Ebola hemorrhagic fever shows early onset of viral symptoms. with a high chance for differential diagnosis in early-onset. clinical assessment is key initial way for diagnosis. Therefore, proper future plans should take into consideration. Ebola hemorrhagic fever suspicion in patient having fever above 38^0cwith the symptoms mentioned and shows trip to an affected area, if present with fever and associated constitutional symptoms. Diagnosis could be difficult since there could be other serious and unidentified diseases can cause in areas of Ebola virus, with the most commonly be malaria and typhoid fever also such as bacillary dysentery., meningococcemia, bubonic plague, Canefield Fever, charbon, relapsing fever, typhus etc.[38] RT-PCR tests were the establishment of the research facility reaction during the 2013–16 west African Ebola infection illness flare-up, although, for many years, the Detection method of filoviruses IS virus isolation in cell culture. when Ebola virus disease patient visit at a hospital, typically one week after the symptoms, the viral effect is already high and identified in the patient's blood byReverse transcription polymerase chain reaction technique in the majority of cases.[39]The diagnosis of ebolaviruses is based on direct identification of the viral particles, proteins or specific RNA in a suspected case from whole blood (WB), serum or plasma.[40] Confirmation of EBOV can only be obtained by virus isolation.[41] However, other investigations such as electron microscopy, histological techniques and specific detection of nucleic acid, immunofluorescence and immunoassays of both antigen and antibodies assume to be positive identification; an orthogonal approach using multiple assay types can be used to increase trust in results. Individual IgM immune response can also be used as a diagnosticcriteria but this is usually only performed during the convalescent phase of the illness; IgG is commonly used for epidemiological surveillance. [42-44]

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Diagnostic Tests [45-46]	
Infection Time	**Available Tests**
In few days after symptoms persist	Antigen-capture enzyme-linked immunosorbent **assay** testing (ELISA)
	IgM ELISA
	Polymerase chain reaction
	Isolation of Virus
Post Recovery	Immunoglobulin M and ImmunoglobulinG antibodies
Backdated in expired patients	Immunohistochemistry testing
	Polymerase chain reaction
	Isolation of Virus

TREATMENT:

Ebola Treatment Facilities have been often exhausted with the number of patients, skilled people were lacking and inadequate staff. While Treating EVD patients, requires the knowledge and proper understanding of the underneath risk of EBD, proper training in infection prevention, control measures and ability to work in any atmospheric situation particularly in heat and humidity with wearing complete personal protective equipment.[47] Currently no any exact treatment for Ebola Virus Disease. Extra care with special attention to liquid intake, management of electrolyte and circulatory function maintenance is suggested. Any operational activity and drugswhich result in bleeding should be considered against the potential benefits and risks for patient. Replacement of blood coagulating factors and platelets may be required. Recuperated male patient should be informed regarding the danger of sexual transmission to partners for at least 90days after recuperation, based on isolation of virus from the semen of 2 months and 12 days after disease onset and of viral sequences 3 months post symptom onset.[48] Most popular strategies for EBOV therapeutics is antivirals that directly target critical stages with binding and/or entry of the virus into cells of host, viral replication, packaging, or release of viral progeny from target cells. Small molecules, antisense therapies, and immunotherapeutics comprise the diverse list of EBOV antiviral compounds.[49-51] The chief Drug that is used in the symptomatic treatment of Ebola virus are: Belladonna, Arsenic, Nitric acid, Aconite, Gelsemium, Bryonia.[52] Two promising vaccines have been reported against EVD till date. GlaxoSmithKline and The United State of America National Institute of Allergy and Infectious Diseases have developed one promising EVD vaccine (i.e. cAd3-EBO Z) is a chimp derived vaccine consists adenovirus vector in which Ebola virus gene was previously inserted. A Winnipeg based health agency of Canada has developed the second vaccine known as rVSVZEBOV. The clinical availability of these vaccines is expectedly to be beginning soon. ZMapp contains 3 monoclonal antibodies; the drug is designed to prevent the EBOV infection in monkeys by neutralizing the GP protein of Ebola virus.[53]

PREVENTION:

Since Ebola virus infection is highly infectious and easily transmitted and there are no standard treatments for Ebola Virus Disease, Separation of infected individuals is very important. If a diagnosis of Ebola is being suspected, then, the patient should be quarantined in a single room with all the facilities, and also a healthcare personnel appointed to take care of patient, healthcare personnel should follow all necessary standard, contact, and droplet precautions, also the use of accurate personal protective equipment (PPE). PPE should include double gloves, N95 face mask,double gown or coverall and apron, eye protection (goggles or face shield) head cover, and

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boots.[43] The risk of spread in infection increases as the contact increase as disease circulate rapidly. During 1976 Sudan EBOV (SEBOV) outbreak showed that 81% of population working as a healthcare provider they infected patient, while only 23% of family members resting in same block with the diseased patients.[54] Furthermore, lack of awareness leading to risky behavior of uneducated people and professionals as well as ignorance of standard procedures and failure of public health system (including crowded emergency rooms, delay in isolation and long-lasting diagnostic procedures, and, finally, low number of health staff), all results in unexpectedly fast spreading of EBOV epidemic.[55]

People should be informed of the following:

I. Preventive measuretaken inanimal-to human transmission:
Prohibit direct contact with animals like bats, hen, chimps, etc and consumption of raw meat.

II. Preventive measure taken in human-to human transmission:
Take proper precautions or to maintain safe distance with people having Ebola symptoms. Appropriate PPE kit should be worn while taking care of patient. Hands should be washed after handling Ebola patients in hospital or home.

III. Preventive measures taken in sexual transmission:
Once the symptoms of EBV is diagnosed by male survivor or by female then they have to take certain precautions during sex and to take proper hygiene condition for at least1year or using a PCR, testing can be done at 90 days of onset of Ebola Virus symptoms and then testing rate is decreased by30 days till their semen tests negative for the Ebolavirus on 2 separate interval at least 1 week difference. During this time, healthcare workers should counsel the patient who suffering from the Ebola Virus and their partner and give some necessary taken actions for safe sex.

IV. Preventive measures to contain outbreaks:
This incorporates recognizable proof of individuals who have been in contact with an EVD patient and checking them for 21 days, rehearsing safe internment of the dead, partition of sound people from the Ebola patients to forestall transmission, and rehearsing great cleanliness while keeping up clean condition.[56]

CONCLUSION:

Ebolavirus Infection is uncommon however hazardous and has no restrictions if episodes are not contained. Nonetheless, if suitable activities are altogether and quickly taken, its transmission can be forestalled and controlled, particularly given the adequacy of the current tools, including the new vaccine.

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