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Review Article

Brief Informative Epidemiological Database Mapping on the Outbreak of Ebola Virus in Africa

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Abstract: Ebola has become a major medical concern in the last few years in Africa and the year 2014 was called Ebola epidemic year. Even till now, physicians and researchers are not able to find out the effective treatment of this epidemic. Ebola hemorrhagic fever is a rare and fatal disease which is also caused by one of the species of Ebola virus. It is supposed to be fruit bats are the most likely reservoir of the various species of this virus. Ebola virus has five different species out of which four occur in the native African animal host (fruit bats) that is why first outbreak of this lethal virus occurred in the following countries of Africa: Demographic republic of Congo, Gabon, Ivory Coast, south Sudan, Uganda, Republic of Congo and South Africa. Diagnosis of Ebola virus is difficult because early symptoms such as high grade fever only which is often seen in patients of malaria and typhoid fever. Researchers are doing their best to find out the specific treatment of the diseases caused by Ebola and putting best effort in developing the FDA (Food and Drug administration) approved vaccine. The motive of present case study on Ebola virus is to provide essential information about the virus and entire epidemic from the beginning outbreak year of Ebola (1976) to till now which might be supposed to be proved useful theoretical medical database to minimize the maximum possibility of lethal effects caused by virus.

Keywords: Ebola, Africa, Epidemic, Ebola virus.

INTRODUCTION

According to Baltimore classification System Ebola virus belongs to Group V (negative (-) ss RNA), order- Mononegavirales and Family name- Filoviridae, also known as Filovirus. The viruses in this order have similar genomic organization and replication tactics and diverge from common ancestor (Fig. 1) [1].

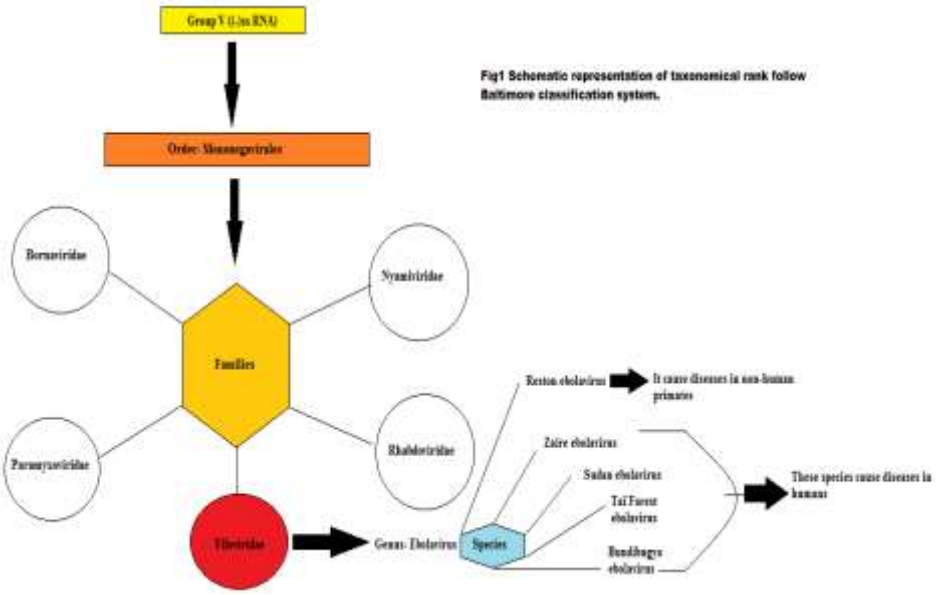

Fig. 1: Schematic representation of Taxonomical rank follows Baltimore classification System [1]

Filoviridae basically includes viruses that form filamentous infectious viral particles called Virons and encode their genome in the form of single stranded negative sense RNA [1]. Ebola virus belongs to Genus Ebolavirus and has five identified species namely Zaire ebolavirus, Sudan Ebolavirus, Tai forest ebolavirus, Bundibugyo ebolavirus and Reston ebolavirus. First four of which cause diseases EVD in humans and fifth one cause diseases in non-human primates (Gorilla, Chimpanzees and Monkey) [1, 2]. It was first discovered in year 1976 near the Ebola River is today now a demographic republic of Congo. Since that year the outbreak began to start [1]. The 2014 outbreak of EVD in West Africa, caused by Ebola virus (*Zaire ebolavirus* species), is the largest outbreak of EVD in history [2]. Ebolavirus cause severe hemorrhagic fever having lethality 50-90% is a highly virulent pathogen [1, 2]. According to centers for diseases control and prevention (CDC) the Filovirus (Ebola and Marburg) are come under Category A of bioterror agent as they can easily transmitted from person to person, might cause public social disruption and public panic and also cause high mortality rate.

STRUCTURE OF EBOLA VIRUS

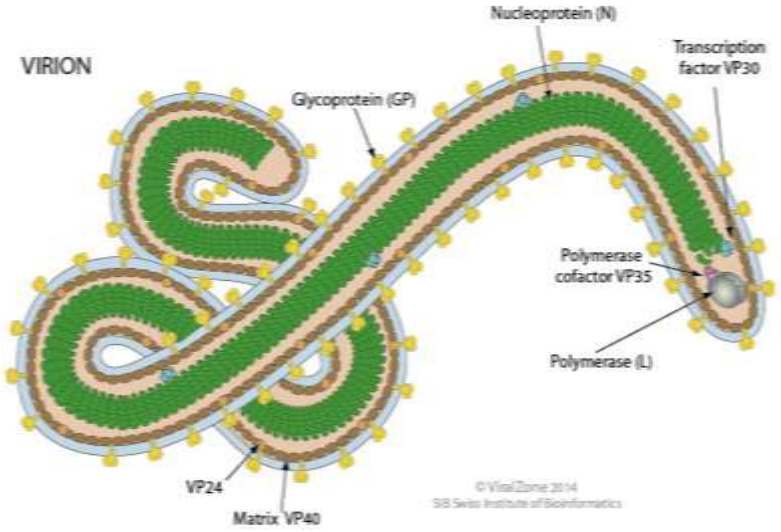

Fig. 2: Shows the seven viral proteins associated the Ebola Virus (copyright Viral Zone 2014 SIB Swiss Institute of Bioinformatics) **[3]**

The Ebola virus genome which is negative sense single stranded RNA is approximately 90Kb in length, which encodes for structural proteins namely [3]. Nucleoprotein is associated with viral negative sense single stranded RNA genome and unite together into helical nucleocapsid (NC) along with polymerase cofactor (VP35), the transcription activator (VP 30) and the RNA dependent RNA polymerase (L) [3-7]. The viral proteins are accounted to be associated for the nucleocapsid catalyzed the transcription and replication of the viral genome [8]. Transcription activators, VP40 is a major matrix protein and VP24 is a minor viral matrix protein is also required for nucleocapsid assembly. If nucleoprotein is expressed alone in the cells, it is attached with cellular RNA to form loose coil-like structure [3,7-12]. The virus gene encode for two form of glycoprotein namely: secreted glycoprotein (sGP) and glycoprotein (GP) and basically small, dimeric, non structural soluble form which function remain unknown and is transcribed directly from viral mRNA [13-16].

This protein is not found in viral identity but secreted by infected cells into the blood [17]. The second one (GP) is basically accumulated by the transcriptional editing of glycoprotein origin of replication and encode a trimeric, membrane bound form. The second one (GP) assemble over the surface to cover the viral entity by forming spike like structures these spikes(GP) are actually expressed over the cell surface and incorporated into Virons to promote viral attachment and membrane fusion [19]. The main terror for Ebola pathogenicity is supposed to be caused by these spikes covering the surface of virus [18]. (GP) post –translational cleaved by proprotein convertase furine to linked disulphide link GP1 and GP2 subunits. GP1 permit viral entity to attach to host cell on other hand GP2 participate in carry out fusion of viral and host cell membrane [19]. This protein assembles as a trimer of heterodimers on the viral envelope, and ultimately undergoes an irreversible conformation change to merge the two membranes [20]. It is co-expressed with VP24 and VP35 to form Nucleocapsid like structures in the cytoplasm that are morphologically identical as seen in infected cells. The gene order in negative sense RNA is as follows: 3′ – leader – NP – VP35 – VP40 – GP/sGP – VP30 – VP24 – L – trailer – 5′ [13, 16, 19]. The trailer and leader regions are not

transcribed, but carry important signals that control transcription, replication and packaging of the genome into new virions. Each gene of viral protein contain their own respective open reading frame as well as long non-translated sequences of undefined purpose that flank the coding regions (Fig 3) [20].

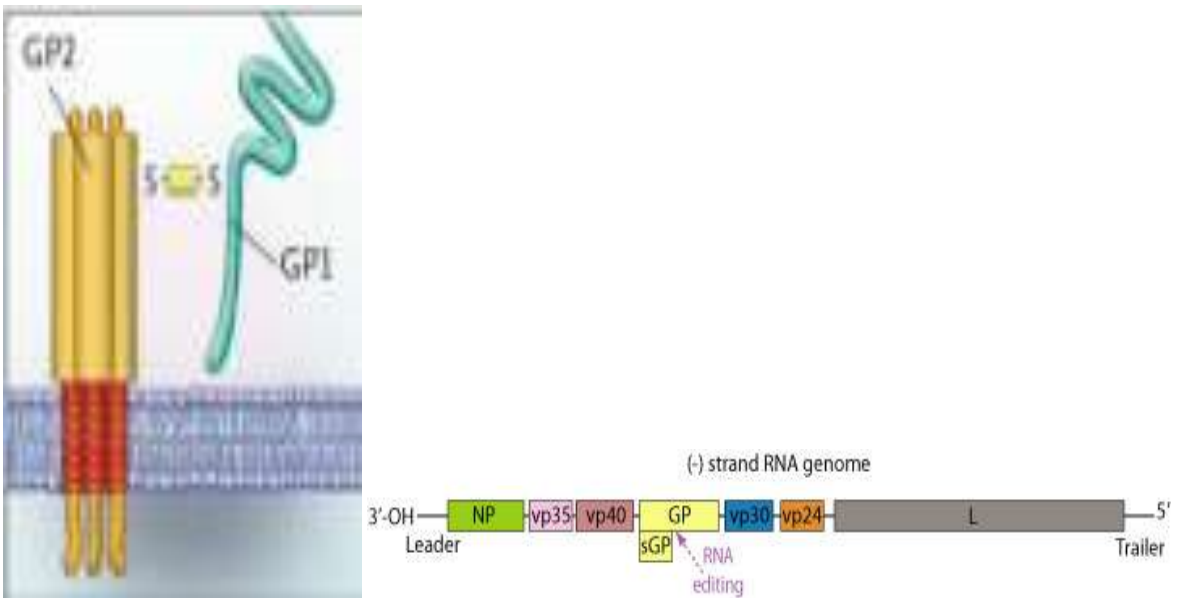

Fig. 3: Association of proteins and disulphide link between GP1 and GP2 subunits [22]

The VP40 encoded in viral genome (third gene) help in maintain structural integrity of virus present beneath the viral envelope containing GP (glycoprotein). It has the ability to induce its own release from the cells in the absence of all other viral proteins encoded in the genome that is why mediate Filovirus budding and also associated with late endosomes [16, 21, 22]. The second minor matrix protein which encoded in viral genome as VP24 (sixth gene) is responsible for suppress interferon production. It also noticed from the other experiment carried out by researchers is that the interferon suppression is not only the main function of VP24 however along with NP and VP35 it also responsible in the formation of nucleocapsid structure [23-25]. It is necessary for the correct assembly of functional nucleocapsid [25-29]. Lack of VP 24 leads to reduce transcription/translation of VP30 [30-33]. The remaining structural proteins form the nucleocapsid, and intimately associated with the single stranded negative sense RNA containing genome. These are Nucleoprotein, Polymerase Cofactor VP35, the viral-specific transcription activator VP30 and viral RNA polymerase L. The structural protein present in the nucleocapsid has the dual function in nature first function is as name indicate structural components and second one is the work as catalyst in the replication and transcription of genome. NP, VP35 and RNA nuclease L are sufficient for Replication but VP 30 is required for transcription initiation without it the transcription will not takes place (Fig. 3) [25,34-36].

TRANSMISSION

The first person was infected through contact with any infected animal which is known as spillover event [33, 34]. Spillover is the moment when a new virus has the opportunity to leap from a bat, monkey or rodent into its first human victim [35-38].

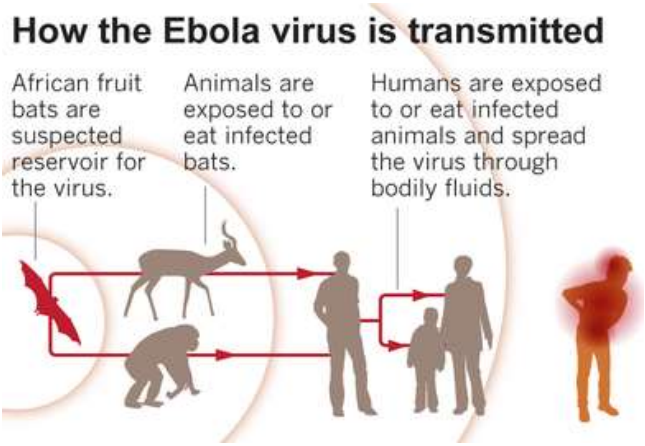

Fig. 4: Shown the Ebola virus transmission by the means of Spillover event [35]

The human to human transmission of virus Occur through broken skin, or mucous membranes in the eyes, nose, or mouth (direct contact), blood or body fluids (urine, saliva, sweat, feces, vomit, breast milk, and semen) of a sick person having Ebola, syringes and needles that have been contaminated with the virus, infected fruit bats or primates (apes and monkeys). It could be spread as a result of handling bush meat (wild animals hunted for food) [35,38-41]. Various reported cases in West Africa are given graphically in Fig. 5-8 [34].

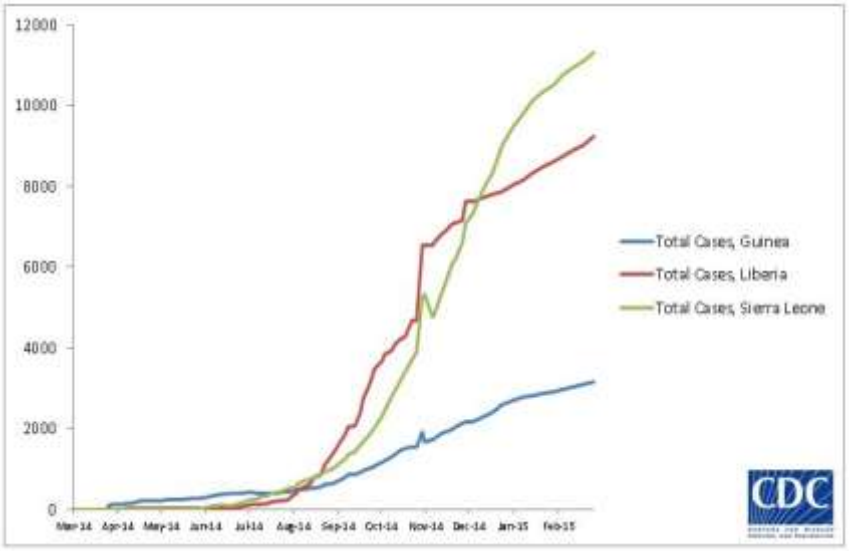

Fig. 5: Total suspected, probable, and confirmed cases of Ebola virus disease in Guinea, Liberia, and Sierra Leone, March 25, 2014 – March 1, 2015, by date of WHO Situation Report, n=23934

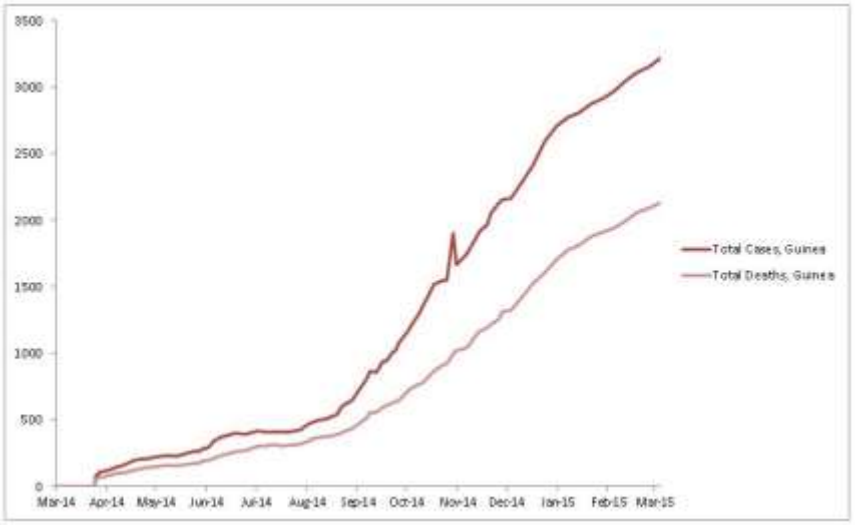

Fig. 6: Total suspected, probable, and confirmed cases and deaths of Ebola virus disease in Guinea, March 25, 2014 – March 1, 2015, by date of WHO Situation Report, n=3219

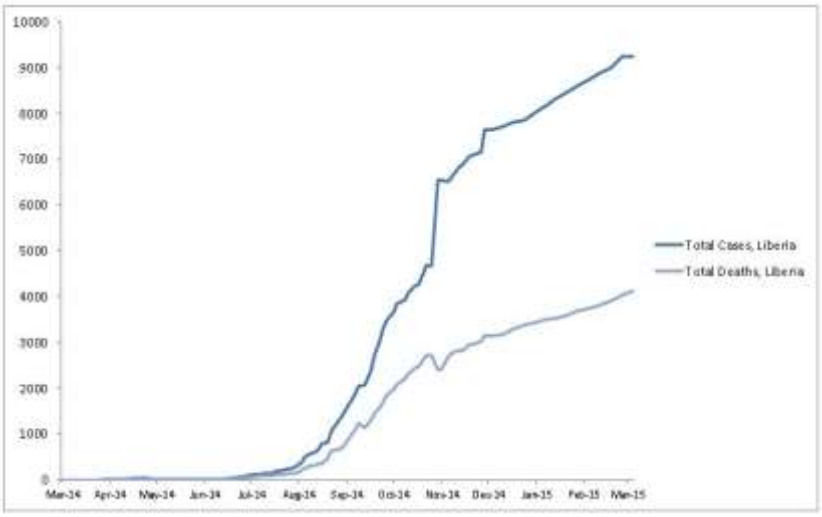

Fig. 7: Graph 4: Total suspected, probable, and confirmed cases and deaths of Ebola virus disease in Sierra Leone, March 25, 2014 – March 1, 2015, by date of WHO Situation Report, n=11466

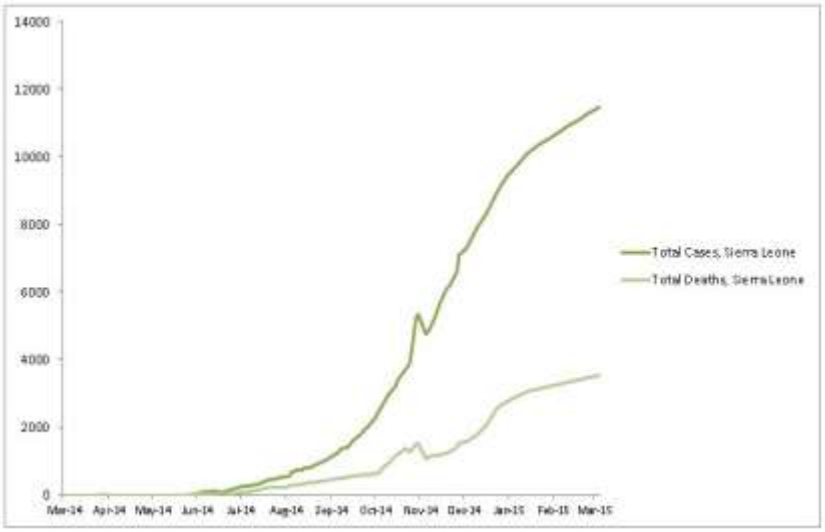

Fig. 8: Total suspected, probable, and confirmed cases and deaths of Ebola virus disease in Liberia, March 25, 2014 – March 1, 2015, by date of WHO Situation Report, n=9249

PATHOGENESIS

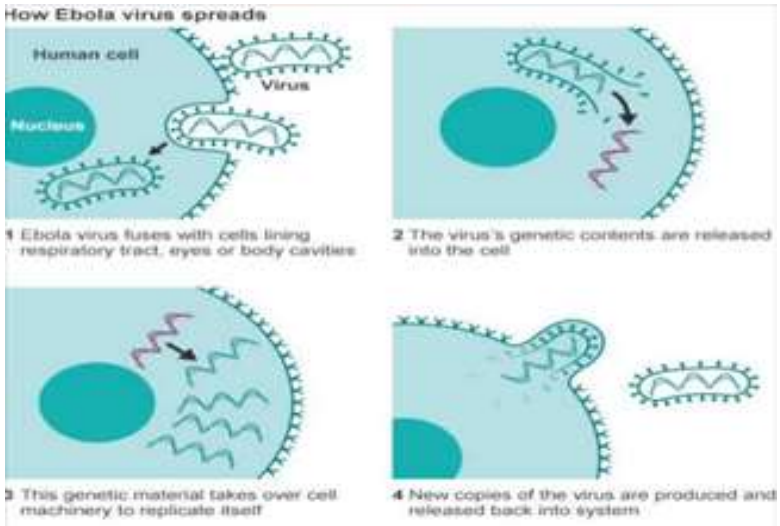

Fig. 9: Diagram shows the pathogenesis of virus [27]

Once the virus enter the human body, the virus encounter the macrophages/monocytes which has trust on host antibodies and compliment system protein C1 (factor) for efficient infection [27, 42]. The WBCs (White blood cells) give response by producing large amount of proinflammatory cytokines that result in increase in permeability of the vascular endothelium, which make easier entry into endothelial cells that are virus secondary target. These proinflammatory cytokines also recruit more macrophage to the secondary target area and hepatocyte (liver cells) being destroyed by the virus. As cytokines recruit more macrophage it also enable virus to spread maximum throughout the body [30, 42, 43]. Ebola virus enters into the endothelial cell by the process called macropinocytosis. Macropinosome move deeply into the cytoplasm to fuse with other vesicles of the standard endolysosomal pathway. This eventually moves the virus into more acidic compartments like early and late endosomes. The infected cell loses contact with the basement membrane and detaches from its neighbor cells by the help of glycan mediated steric occlusion by GP [31]. The newly created particles then leave through lipid rafts, leaving a destabilized vascular system responsible for the massive blood loss characteristic of Ebola patients [32]. On the other phase of the infection, the immune system of the body become out of control. VP35 interfere in interferon production nearly at every step of the process [34]. Secreted Glycoprotein (sGP) limits the movement of WBCs as these are trapped inside the circulatory system. Proinflammatory cytokines that destroyed the vascular endothelium is released by macrophages/monocytes. Macrophages/monocytes also responsible for activating coagulation cascade [42]. The conditions put the human body into paradoxical condition in which the patient can die by from catastrophic thrombosism, by the hypovolemic shock from massive hemorrhage or the formation of blood clots around the body [34].

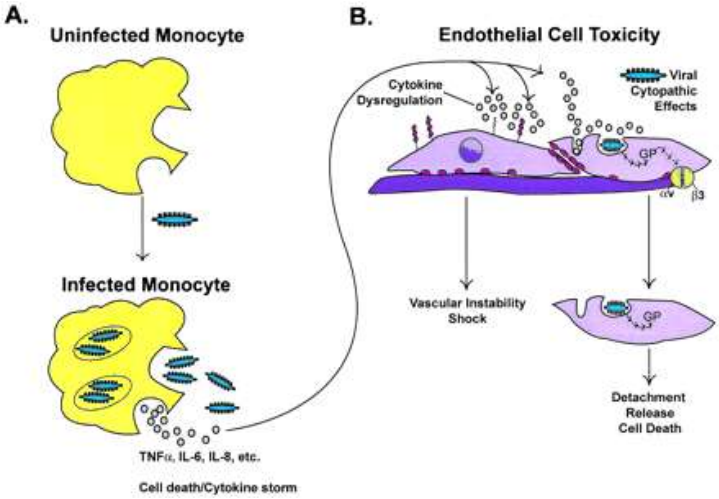

Fig. 10: Ebola virus causes destabilization of the vascular endothelium leading to hemorrhage [41]

PREVENTION

Keep following precautions to be taken:

- Maintain hygiene as the virus is contagious for example always wash your hand with alcohol based hand sanitizer, soap and water, avoid contact with body fluid like saliva, plasma and blood serum.
- Always maintain distance with the item that comes in contact with infected person's blood or body fluids (such as bleedings, medical equipments, needles, clothes).
- Always try to avoid participating in funeral or burial rituals of the person as the virus is contagious.
- Keep distance with bats, non human primates, raw meat prepared from the animals.
- Avoid using medical facilities in West Africa where Ebola patient are being treated. The U.S embassy or consulate is often able to provide advice or facilities.
- Monitor your health for at least 21 days and do medical care immediately if you find any symptom of the Ebola. [34,38-41]

Healthcare workers have to follow these steps:

- Wear appropriate personal protective equipment (PPE).
- Practice proper infection control and sterilization measures,
- Isolate patients with Ebola from other patients,
- Avoid direct, unprotected contact with the bodies of people who have died from Ebola.
- Notify health officials if you have had direct contact with the blood or body fluids, such as but not limited to, feces, saliva, urine, vomit, and semen of a person who is sick with Ebola. The virus can enter the body through broken skin or unprotected mucous membranes e.g. eyes, nose or mouth [38-41].

DIAGONOSIS

The virus is detected after onset of symptoms in patient, most notably fever, which accompany the rise in circulating virus within the patient's body. It usually takes up to three days after symptoms start for the virus to reach detectable levels (Table 1) [41].

Table 1: Laboratory tests used in diagnosis

Timeline of Infection	Diagnostic tests available
Within a few days after symptoms begin	• Antigen-capture enzyme-linked immunosorbent assay (ELISA) testing • IgM ELISA • Polymerase chain reaction (PCR) • Virus isolation
Later in disease course or after recovery	• IgM and IgG antibodies
Retrospectively in deceased patients	• Immunohistochemistry testing • PCR • Virus isolation

TREATMENT

Symptoms of Ebola and complications are treated as they appear. The following basic interventions, when used early, can significantly improve the chances of survival: Providing intravenous fluids (IV) and balancing electrolytes (body salts), Maintaining oxygen status and blood pressure, Treating other infections if they occur. Experimental vaccines and treatments for Ebola are under development, but they have not yet been fully tested for safety or effectiveness. Recovery from Ebola depends on good supportive care and the patient's immune response. People who recover from Ebola infection develop antibodies that last for at least 10 years, possibly longer. It is not known if people who recover are immune for life or if they can become infected with a different species of Ebola. Some people who have recovered from Ebola have developed long-term complications, such as joint and vision problems [41].

*No FDA-approved vaccine or medicine (e.g., antiviral drug) is available for Ebola [41]

CONCLUSION

From this case study it was found that Ebola virus is highly contagious and a big medical lethal challenge. We have to follow the guidelines of governing body like "WHO" (Word health organization) CDC (center for diseases control and preventions). Diagnosis tests are available for the infection caused by Ebola-virus after the onset of symptoms: Antigen-capture enzyme linked immunosorbent assay (ELISA) testing, IgM ELISA, Polymerase chain reaction, Virus isolation is preferable; later in diseases course or after recovery: IgM and IgG antibodies is preferable and retrospectively in diseased patient: Immunohistochemistry testing, PCR, virus isolation is preferable. Always maintain Hygiene.

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