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LASSA OR EBOLA: THE THREAT OF THE NEXT HUMAN PANDEMIC

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Abstract

LASV and EBOV are the two emerging zoonotic pathogens that caused an infection that results in a severe hemorrhagic fever (HF) in the people of Africa. Both Viruses have been reported more than 40 years ago, i.e. 1969 and 1976. It has been estimated that LASV is continuously emerging with more than 5 million cases and 5,000 deaths every year, whereas, until today, EBOV is responsible for a total of eleven outbreaks with more than 30, 000 cases and 15,000 deaths. However, Both Viruses re-emerging with more severity, fatality, and asymptomatic condition than previous, which is creating a considerable situation in the current world's battle of SARS-Cov-2 pandemic. Therefore, our current review article aims to hypothesize the upcoming global outbreak of LASV or EBOV based on their current Immune genesis, pathogenesis, and epidemiological understanding. However, our understanding of pandemic and disease spreading of both viruses are limited, particularly the environmental factors that contribute, and the cellular and viral dynamics during transmission from natural reservoirs to humans, and last, the virology in humans is quite complicated. Therefore, improvement in the scientific collaboration and research activities, funding for projects, and encouragement of health ministries and the research institutes are necessary for better understanding the viruses. In last, a data-sharing platform should introduce for all researchers having an opportunity to share and conceptualized all the necessary materials related to pathogens, such as epigenetics, host-factor, genomics, and proteomics, which will contribute as an advantageous step towards the battle against Lassa or Ebola viruses.

Keywords: *LASV, EBOV, Pandemic, Hemorrhagic, Fever, Covid-19*

INTRODUCTION

LASV and EBOV have been originated from two different families known as Arenaviridae and Filoviridae. They are now well thought out zoonotic pathogens, due to their potency to cause hemorrhage fever (HF) in people of Africa. They are now considered a big alert to the health of the public because of their high potential of human-to-human infection and spreading [1].Both viruses were reported more than 40 years, in 1969 the initial incident of the Lassa virus occurred when two missionary nurses had been died due to an unknown disease, they were performing their duties in the Lassa town of Nigeria [2]. The pandemic is circulating in West African countries such as Sierra Leone, Guinea, Liberia, and Nigeria, respectively, but some of the neighboring countries including Ghana, Burkina Faso, Mali, and lvory Coast were also infected by transmission [3]. A multimammate rodent known as Mastomys natalensis is proposed as the primary reservoir host for Lassa, whereas,

Hylomyscus pamfi and Mastomys erythroleucus are secondary hosts reservoir [4]. The fourth rodent species reservoir of LASV is M. baoulei pygmy mice [5].

The Ebola virus outbreak initially occurred following seven-year of LASV (1976) in the closest area of the Ebola River in the Democratic Republic of Congo (DRC). Approximately 284 persons with 53% of mortality were wrapped by this outbreak. There is no accurate information about the Ebola virus reservoir, but the fruit bats are known as Hypsignathus monstrous and Epomops franqueti are considered to be the primary host [6].

Currently, the world has convoluted by the Covid-19 disease. Which is originated in Wuhan city of China, but continued to spread among cities in china and finally worldwide [7]. On March 11, 2020, the WHO declared Covid-19 a pandemic and reported approximately 1.5 hundred million cases and 3 million deaths on April 30, 2021 (WHO 2020 and 2021). In Nigeria, during this critical situation, the LASV has also emerged with 4622 suspected while 991 confirmed cases, with a total of 191 deaths reported on May 8, 2020 (NCDC 2020). Similarly, the 10th Ebola outbreak also occurred between 2018-2020, killed 2300 people with 3481 suspected cases in DRC [8]. Further, new Ebola cases have also been recognized in DRC and guinea (WHO 2021). Therefore, by looking at the continuously re-emerging of LASV and EBOV outbreaks with more severity, mortality, and the existence of an asymptomatic condition of the patients, we hypothesized the upcoming global outbreak of LASV or EBOV based on their current Immune genesis, pathogenesis, and epidemiological understanding.

THE BIOLOGY OF LASV AND EBOV

Although Lassa and Ebola have been originated from two different families but they are showing many similarities in their biological composition. The helical nucleocapsid genome of the Lassa Virus consists of two negative segments of RNAs which are covered by double layers of lipid molecules and glycoprotein spikes on the surface. Each segment RNA encodes two different components, the small RNA encodes the nucleoprotein NP with the size of 60 kDa and glycoprotein precursor in immature form (pre-GP-C) with the size of 80 kDa, which is further synthesized into GP-C (75kDa) and a stable signal peptide of 58 amino acids (aa) through co-translation cleavage by signal peptidase [9]. The GP-C is then converted into envelope protein that is involved in the attachment of virus and cell entry. In the meantime, GP-C is post-translational cleaved into GP-1 N-terminal subunit and Gp-2 membrane-bound subunit by subtilase Ski-1/S1P, the particles of the virus incorporate by both subunits [10].

The structural protein nucleocapsid (NP) acts as an important role in the viral RNA replication and transcription and assembly of the virion [11]. It is also interrupted in the production of type I interferon signals against the viral genome [12]. The NP domains of the Lassa virus also contain the N- and the C-terminals, same as other viruses NPs. However, there is no known viral NPs similar in domain structure to Lassa [10]. The “C” domain of Lassa NP consists of exoribonuclease activity which performs a role in the degradation of pathogen-associated molecular patterns (PAMP) RNA ligands. The RNA ligand induces to produce type I interferon signals by different cellular pattern-recognition receptors (PRRs) after detection of the virus attached to the receptors [13].

The large segment of RNA involved in the encoding of L (200 kDa) and the Z protein (11kDa) having a length of 99 amino acids**.** The RNA dependent RNA polymerase (RdRp) activity is present in the central region from residues 1040-1540 amino acid of L-protein [14]. The 250 kDa L-protein plays the main role during the process of transcription and replication of the viral genome. Some experiments are reported that “RdRp” and specific amino acids in C-terminus are crucially necessary only for

transcription of the virus but not replication [15]. Moreover, the N-terminus is also necessary for the synthesis of mRNA [16]. The Z-protein is required for assembly and viral-like particles releasing. Z-protein consists of two domains known as late domains that contribute to the spreading of virus particles throughout the cell membrane.

Lassa virus is used glycoprotein's GP1 extracellular spikes for the attachment to the a-dystroglycan (a-DG) protein to initiate infection in the host, DG is an extracellular protein that is connected extracellular matrix to the actin cytoskeleton through the transmembrane ß-dystroglycan [17] The endocytosis begins once a Virion binds to the surface of the cell, the Virion travels to the endosomal system of the host cell [18]. Later, due to the acidic pH of endosomes, GP1 changes its target from a-DG into lysosomal-associated membrane protein-1 (LAMP-1), the viral particles are now allowed for releasing its materials into the cytoplasm after fusing with the remaining lysosome that begun because of structural changes in the host cell [19].

On the other hand, Like the LASV, The Ebola virus (EBOV) is also consist of a negative Stranded RNA genome which codes a Nuclear Protein (NP), Glycoprotein (GP), and four structural proteins called viral protein24, Viral Protein30, Viral Protein 35, and Viral Protein 40. Ebola is an enveloped filamentous virus. NP, VP35, and L-protein are responsible for viral replication. The active polymerase complex consists of Viral Protein 35 (polymerase factor) & L (polymerase). Nuclear Protein is responsible for RNA encapsulation [20]. Viral Protein 30 is a transcription stimulator that plays a role in forming and constructing nucleocapsids [21]. VP24 is a matrix protein that is also involved in nucleocapsid formation, while VP40 matrix protein promotes progeny virions budding in infected cells [22]. Glycoproteins (GP) are surrounded by virions and perform a vital role during EBOV attachment to the host [23]. Spikes shapes are composed by GP and having a size of 7nm and are separated with 5-10 nm on the surface of virions [24]. DNA editing data showed two soluble forms of GP, sGP, and ssGP [25]. Nonstructural Secreted GP (sGP) is encoded by well-conserved primary ORF of GP genes on 264 residues [26]. Which is further cleaved proteolytically from the pre-sGP form into the mature sGP by furin and a small, nonstructural secreted protein called Δ-peptide by heavily O-glycosylation [27], though it has illustrated that mature sGP contains six sites for N-linked glycosylation but only five sites are involved in their activities [28] However, the involvement of sGP in pathogenesis is still unclear, but the presence of sGP in high concentration has been determined in the serum analysis of infected person [26]. Moreover, sGP also contributes in resistance to the humoral immune response after antibodies observation produced by the host [29]. In contrast, Non-structural Small sGP (ssGP) is produced by modification of GP with extra adenosine (deletion/addition) during transcriptional errors [30]. It is also not clear that during pathogenesis what could be the participation of ssGP. In short, by studying the biological nature of both LASV and EBOV, the result data proposed that both viruses contain similar biology with most of the other RNA viruses. Consequently, it could be beneficial to reused already practiced technology for the development of vaccines and other therapeutics.

THE PATHOGENESIS AND IMMUNOLOGY OF LASV AND EBOV

Both LASV and EBOV have a similar mechanism of pathogenesis because of their same initial target cells called myeloid cells (macrophages and endothelial cells) and also infection of the same organs. Nonetheless, there are certain dissimilarities in terms of their protection or pathogenesis against specific immune responses that are activated by host cells after infection [31].

Although, Lassa and Ebola virus reservoir hosts are not affected by infection, might be due to their immunosuppression ability, but in human these viruses are causes Hemorrhage fever (HF). The incubation time of Lassa fever has 6-21 while Ebola 2-21 days [32] which start with the symptoms common to flu-like such as fever, weakness, cough, sore throat, and pain in joints, back, chest [33]. Hence, about 80% of the LASV and 46-71% of EBOV victims are showing asymptomatic conditions because of mild infections [34]. Though the whole proportion of LASV mortality is almost low i.e. up to 1% this proportion could increase by approximately 50% during a pandemic, In contrast, EVD is a high mortal rate ranging from 25-90% with approximately 50% of an average and up to 70% of CFRs have also reported during pandemic (WHO October, 2014, WHO September, 2014, WHO December 2014, WHO January 2015). Whereas, the mortality rate in Health workers was 57% during 2013-16 pandemic of EBOV [35]. Healthy Humans could be infected from LASV or Ebola by direct contact to the reservoir or patient body fluids such as urine, feces, blood, and also from meat consumption and inhalation of infected body released aerosol. Aerosol stability of Lassa and Ebola viruses has been reported [36]. However, the naturally aerosol transmission of LASV and EBOV has not been identified between humans yet. But the Nigerian outbreak of Lassa fever in 1970 has been indicated to be related to airborne transmission from a female patient with severe pulmonary disease [37]. Moreover, the in-vitro aerosol transmission of LASV and EBOV between animals has also been determined during experiments [38]. Alpha-dystroglycan (alpha-DG) acts as a receptor for Lassa virus entry, a group of glycosyl transferases known as LARGE protein help in the receptor recognition through sugar modification in alpha-DG [39]. Once LASV enters the body of a human it infects ultimately every tissue, probably begins with lungs, intestine, mucosa and urinary system, and finally the vascular system [40]. Commonly, the innate immunity system detects the pathogen-associated molecular pattern (PAMP) after infection of the pathogen and then induces an immune response [40].

Generally, T-cell performs an important role in the protection of viruses, but the disease can spread once it fails to defend. Regarding in response to LASV protection different mechanisms of T-cell are involved [41]. T-cell response in successful recovered non-human primates is showed strong activation whereas; completely deactivation of T-cell is determined in severely infected animals [42]. Moreover, at the beginning stage of LF disease, the T-cells (CD4+ and CD8+) are strongly activated with continuous detection but antibody response was gradually reduced or completely absent after recovery of the victims [43]. T-cell present epitopes (MHC-I and MHC-II) on infected monocytes or macrophages. A study conducted on the role of T-cell epitopes against the protection of LASV is reporting that MHC-I, acts a more important role in LASV defeatism [43]. The activation of CD4+ T cell in response against to NP and GP of Lassa virus have also been determined in LASV-seropositive healthy persons living in the area of LF pandemic, this evaluating that activation of CD4+ T-cells in healthy persons are also linked with mild and/or non-symptomatic conditions [44,45]. In contrast, T-cell immunoglobulin mucin domain-1 (TIM-1) is considered the receptor for EBOV entry. TIM-1 cells act as a receptor for phosphatidylserine (PS) that facilitates apoptosis of dead or dying cells [46]. Likewise LASV, the EBOV is also infecting and replicates in monocyte, macrophage, and dendritic cells. Monocyte and macrophage infection triggers robust inflammatory mediation expression [47]. These cells including viral particles then passed to lymph nodes and nodal chains through lymphatic vessels to facilitate replication and distribution of viral particles [48]. High-level replication of EBOV in human host are linked in the influence of suppression or over activation of the immune system during different stages of the immune response, which result in disease outcome, tissue damage due

to direct involvement of viral and indirectly host-mediated effectors. The highly frequent replication of EBOV could enhance the multiple organs failure in 10 days of the symptomatic host while in the absence of a proper preventive system [49].

DYSREGULATION OF INNATE IMMUNITY BY EBOLA VIRUS

In order to respond to EBOV, various studies have shown that unregulated secretion of pro-inflammatory cytokines, chemokine, and growth factors, such as IL-1β, IL-6, IL-8, IL-10, MPE-1, MIP-1α, MIP-1β, and TNFα, as well as nitric oxide and reactive oxygen species that, when they die, can range between 5 and 1000 times the detection of the survivors and in healthy people. Early in the outbreak, survivors, on the other hand, display a transient and mild up-regulation of IL-1, IL-6, TNF, MPE-1, and MIP-1. These findings indicate that defense against fatal EBOV infection may be based on a rapid but well-controlled inflammatory response [50]. An interferon reaction of type I is also typically of an Ebola virus and is an element in the Innate Immune Response to viral infections. Viral Protein24 prevents Interferon-induced genetic expression by blocking the STAT1 (pSTAT1) nuclear transportation, a crucial downstream product for IFN signaling. They are usually transported through the nuclear pores of pSTAT1 via the c-terminus of karyopherin protein (Karyopherin 1, 5, and 6), which causes pSTAT1 to fight for a nuclear binding transporter [51]. Furthermore, with the addition of VP24, the VP35 inhibited IFN Regulatory Factor 3 (IRF-3), which resulted in reduced IFN development. [50]. VP35 interacts with Ubc9, the SUMO E2 enzyme, and PIAS1, the E3 ligase, leading to enhanced IRF-7 degradation and SUMOylation. By binding to the RIG-I activating dsRNA22 or PKR activating protein (PACT), VP35 can inhibit the retinoic acid-inducible gene's reported signaling (RIG-I) [50].

EPIDEMIOLOGICAL PERCEPTION OF LASV AND EBOV

Lassa and Ebola are constantly causing hemorrhage fever disease in different areas of West Africa, particularly in Sierra Leone, Guinea, Liberia, and Nigeria. Presently, approximately 3-5 million per year LASV cases and 5,000 deaths have been detected in these four countries [52]. However, the estimation could be crude due to non-uniform surveillance of the real cases of LASV. The last epidemic of LASV occurred in Nigeria during the 2018 transmission season (mainly December 2017 through May 2018), and WHO declared it an outbreak while imposing a level, 2 public health emergency [53]. Nigeria center for disease control has investigated a total of 431 laboratory-confirmed cases from 21 states, containing 37 health workers with approximately 25% of mortality rate [54]. Furthermore, the Nigerian health ministries were demonstrated the previously unknown factors or a new or more virulent strain of LASV responsible for the 2018 outbreak. Later, in the second outbreak from January 1st to March 24, 2019, the number of cases rose with a total of 495 confirmed positive from out of 1924 suspected cases, the mortality rate of the positive cases were 22.9% (NCDC 2019). In 2020, the same estimation was recorded with 1165 confirmed cases. During November 2014-16, A total of 15 confirmed positive cases were recognized in Benin and Togo, two Confirmed positive victims died. Before 2014 this disease did not occur in these countries. In October 2011, three fatal cases were determined in different districts of Ghana, the first infected patient had no record to travel outside the area during his infection period, and however, he usually visited the close forests for hunted rodents (WHO, 2011a,) which, strengthen the reservoir of LASV in rodents in the area.

On the other hand, until today total of eleven outbreaks of EVD occurred in different countries of Central Africa. Recently, another new outbreak is confirmed in DRC and guinea (WHO 2021), as of 18th March of the current year the number of Cases increased to twelfth with six deaths in DRC, while 23 with 11 deaths in Guinea (WHO 2021), whereas the world, is already convoluted by COVID-19 pandemic. Moreover, the previous 10th Ebola outbreak in DRC lasted for approximately two years (August 2018- June 2020) which is considered the second-largest global pandemic.Meanwhile, the world largest outbreak occurred between 2014-2016 following a short outbreak declared in 2013, with more than 28,600 suspected or confirmed cases and 11323 fatal cases (CFRs 46%) [55].

LASV and EVD have been rapidly spread from the pandemic regions to non-pandemic areas of the world during the last decades. This spreading is directly related to the traveling of different bodies such as health workers, missionaries, and foreign military from the epidemic regions.Until 2016, approximately 33 confirmed cases of LASV and 22 of EVD were reported in different countries including the US, UK, Germany, Netherlands, Israel, Japan, Sweden, South Africa, Canada, Spain, Italy, Russia, and the Philippines.The mean age of the victims was 45 years (between 18-72 years) [56]. Meanwhile, before March 2016, a total of 22 LASV cases have been stated in the European Unions (UN) and 8 in the United States (US), in which 8 and 3 patients died from both regions [57].
The imported cases of such viruses into these countries demonstrated the probability of this highly mortal and morbid pathogens to spread by traveling on commercial planes [58]. Apart from this, the lack of proper management by local health authorities to control the outbreak and the existence of international health workers in pandemic areas increased the probabilities of export cases among the public and others people of different departments. Consequently, due to frequent contact of human with reservoir and the international mobility, LASV/Ebola could be an endanger alert for the health of people and national security, which was already assessed with an average of 2.8 export cases per month worldwide during 2014-2016 EVD outbreak [59].

VACCINES PLATFORM FOR LASSA AND EBOLA

Currently, there are no effective vaccines available to prevent Lassa or Ebola. LASV is frequently needed research activities because it could be a Danger threat to public health due to its high ability to cause infection and fatality. In June 2017, in order to develop effective and safe LASV vaccines the WHO referred target product profile (TPP) to make an ease for the scientists (WHO 2017) because only the safe and effective vaccines would control the pandemics. Currently, several vaccines approaches such as DNA, RNA, live attenuated, and multiple different viral vectored vaccine are under the development stage,[60] Until different trials have been applied on rodents and non-human primates' model to check the efficiency and protection of LASV vaccines. One of the leading candidates for the recombinant vesicular stomatitis virus (VSV) vaccine is under fast development by the Coalition for Epidemic Preparedness Innovations (CEPI),[61] who are handling the vaccines candidates' development. Recently, data suggesting the efficacious vaccine candidate term as ChAdOx1-Lassa-GPC vaccine. ChAdOx1 is a platform of a chimpanzee adenovirus vector and has been used in the development of vaccine candidates for various pathogens. Until a single dose of the ChAdOx1-vectored vaccine has been identified to be protective against Rift Valley fever virus, Middle East respiratory syndrome coronavirus, Zika virus, and Mycobacterium tuberculosis in animal models of infection [62]. Likewise, Hartley guinea pigs were also protected from LASV infection by using a single dose of ChAdOx1-Lassa-GPC [63]. Likewise, many platforms have also been created for

the EBOV vaccine. "Replication Deficient Vaccines includes Deoxynucleic acid-based Vaccines, Virus-like Particles (VLP), and Recombinant Adenoviruses (rAd) Vectors. Replication includes Recombinant Human Parainfluenza Virus 3 (rHPIV3), Recombinant Vesicular Stomatitis Virus (VSV), & more newly Recombinant Rabies Virus (RABV) & Recombinant Cytomegalovirus (CMV)." Clinical trials have begun on 38 successful vaccine candidates: pseudo-expressing rAd and rVSV vectors [64]. Recently, Federal Drug Agency (FDA) approved the first Ebola Vaccines term as recombinant vesicular stomatitis virus–Zaire Ebola virus (rVSVΔG- ZEBOV- GP) with brand name Eryebo, which expressed GlycoProtein (GP) of EBOV [65] and is used for protection against Zaire strain. The vaccines showed a reduction in mortality after limited vaccination trials delivered in Guinea in 2015 [66]. Nonetheless, the clinical symptoms of mild EVD are still assessed in some individuals since they received vaccines. There is no accurate data to investigate the reason for such cases, instead of considering the infection of EBOV during the first 10 days after vaccination [67]. Another reason could be the possibility that live attenuated vaccines reconvert to their virulent form which may be the result of serious problems. Thus, it could be a better solution to introduced subunit vaccines that are safer with the insufficient fragment of virulent agent [68].

Despite all of them, the research in the development of LASV/EBOV vaccines has still less interested because of lacking a full understanding of the biological nature of the disease, epidemiology, and also insufficient number and unsatisfied data of experimental animal models [67]. Furthermore, the manufacturers have also less attraction towards the development of vaccines due to less commercial and economical value in comparison to products developmental processing cost [69].

FUTURE RECOMMENDATIONS AND PERCEPTIONS

LASV and EBOV have frequently reoccurred from unknown sources in western Africa, for the last 40 years. However, our understanding of pandemic and disease spreading of both viruses are limited, particularly the environmental factors that contribute, and the cellular and viral dynamics during transmission from natural reservoirs to humans and in last the virology in humans are quite intricate. Furthermore, The WHO listed both as category "A" agents and assessed them as bioterrorism threats worldwide, due to their extreme virulence and mortality. Hence, the primary reservoirs are considered to be the rodent species M. natalensis for LASV, while bat species Hypsignathus monstrosus and Epomops franqueti for EBOV (As discussed in the introduction), with these some species of ebola virus-like Reston and Zaire have also been identified in bats from different Asian countries such as Philippines, China, and Bangladesh. Among them, the Philippines *Reston Ebola virus* (REBOV) in the reservoir *Rousettus amplexicaudatus* is associating with the potential reservoir host for this virus in Asia. In addition, some European countries including France, Spain, and Portugal have also investigated bats are potential reservoirs for filovirus, for example, *Miniopterus schreibersii*, is identified reservoir for filovirus term as Llvoiu virus died after viral pneumonia, however, the morbidity of the virus in human is until unknown. Nonetheless, the discovery of the virus was significant due to the identification of filovirus outside of Africa and Asia. On the other hand, the LASV reservoirs are the rodents of Muridae family. Interestingly, most of the viruses belong to the mammarena genus are associated with rodents hosts, for example, *Whitewater Arroyo virus, Junin Virus, Chapare Virus, Flexal Virus, Guanarito Virus (GTOV), LCMV, and* WENV, Isolated in Argentina, USA, Brazil, Venezuela, and China, addition with these, the LCMV species has globally spread almost in all contents, except Antarctica, Strengthen the possibility for LASV and EBOV to spread globally because of the movement of rodents/fruits bats for struggling to survival in

ecological changes, or due to new reservoirs in non-epidemic areas. Furthermore, the natural reservoir for the current global COVID-19 epidemic originated in Wuhan, China is also thought to be the bat animal, prompted that consumption and hunting of Bats or Rodents could be the source of EBOV or LASV outbreak, as different species of filovirus or mammarenavirus have already been investigated in these reservoirs in china. Generally, the mortality of Covid-19 (~2%) is higher than LASV (usually 1%) but less than Ebola (Average 50%), however, the lethality may rise during pandemics. Thus, it necessary to be granted precautionary countermeasure before it is too late, for example, to speed up the scientific research activities, the funding, and awareness of health ministers and research institutes for a better understanding of the viruses. Before the new biological war begins, it is strictly required to take up some steps that eventually controlled the spreading of both viruses from animals to humans and then transmission between humans in the future. Particularly, aggressive countermeasures should substantialize for Ebola restriction, as the virus re-emerged with high fatality even from the current lethal SARS-Cov2.

The most important precautionary approach to such endemic agents is to exercise the community by preventive molecules such as vaccines, however, the re-emerging of LASV or EBOV outbreaks occurs with new strain and also without prediction of places and times. Interfering in the development of efficacious vaccines, for this, transitional knowledge is acquired to understand the entire mechanisms of diseases to facilitate the designing and discovery of "Universal" vaccines for the prevention of further outbreaks. But then, it will take a longer time to developed Universal vaccines or other therapeutic drugs. Therefore, protruding of certain precautionary measures should be considered to prevent the next outbreak globally, for example, the disease should constrain limits only to the endemic areas, reservoirs control and deterrence to their excretes etc. Nevertheless, it could be arduous to do so, because of the existence of carrier pathogens in non-symptomatic conditions, even the sexual transmission of the Ebola virus has recently been investigated in a woman having sexual intercourse with a man following 1-1.5 year of disease recovery. Last but not least, the control strategies of such outbreaks need strict surveillance, Responses of public health, and mutual understanding between health workers, medical staff, and social people. Besides this, a strong and well infrastructure health system should be considered to carefully monitor the origin of spillover transmission from zoonotic pathogen into human society. Furthermore, awareness of the public, education, and training of health workers for universal precaution, as well as potential surveillance of airline passengers is associated to overcome an eventual outbreak. In last, it should under consideration to provide a platform for all the researcher has an opportunity to share and conceptualized all the necessary materials related to pathogens, for example, information of epigenetics, host-factor, genomics, and proteomics, which will contribute as an advantageous step towards the battle against LASV or EBOV.

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