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Lassa Fever: An Emerging and Re-emerging Fatal Viral Disease of Public Health Concern

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Abstract Lassa fever is a life threatening infectious zoonosis of public health significance, and is caused by a single-stranded, linear, bi-segmented RNA virus belonging to the *Arenaviridae* family. The disease is transmitted by rodents, particularly the Natal mastomys (*Mastomys natalensis*). In terms of public health impact, Lassa fever outperforms Ebola, Marburg, and all other hemorrhagic fevers except Dengue. Lassa fever is endemic in Benin, Ghana, Guinea, Liberia, Mali, Sierra Leone, and Nigeria, although it is also thought to exist in other West African countries. Each year, it is thought to be responsible for up to 300,000 new infections and 5000 deaths in Western Africa. Lassa virus disease was named one of the world's top bio-threats by the global Coalition for Epidemic Preparedness (CEPI) in 2017. Humans are most typically infected through the ingestion or inhalation. Nosocomial infection is also noticed. Very recently, an outbreak of Lassa fever was confirmed in Togo. However, when symptomatic, fever, general malaise and weakness, headache, hemorrhaging (in the gums, eyes, or nose, for example), respiratory distress, frequent vomiting, face swelling, discomfort in the chest, back, and abdomen; and shock occur. Deafness is the most common complications of Lassa fever. The fatality rate in the hospitalized patients may reach 15 to 20 %. There are a variety of virus diagnostic techniques available, ranging from viral culture to serological and molecular diagnostic testing. There are currently no FDA-approved vaccinations for Lassa fever, and therapy options are exceedingly restricted. Early supportive care, such as rehydration and symptomatic treatment, improves survival prospects.

Keywords: *emerging disease, Lassa fever, Lassa virus, Mastomys natalensis, public health, Western Africa, zoonosis*

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1. Introduction

Emerging and re-emerging zoonoses of diverse etiologies pose significant impacts on human health and economies globally [1,2]. Lassa fever also known as Lassa hemorrhagic fever is an important zoonosis of public health importance, and is caused by Lassa virus that belongs to the genus *Areavirus* and family *Arenaviridae* [3]. The disease is endemic in West Africa. Annual epidemics primarily affect the rural population during the dry season [4]. In 1969, the virus was isolated from the bodies of two missionary nurses who died of Lassa fever in Nigeria [5]. Lassa virus has a single-stranded, negative-sense, bisegmented RNA genome. Lassa virus is endemic in Western Africa, particularly in Nigeria, Liberia, Guinea, and Sierra Leone, where it is primarily transmitted by the multimammate rat (*Mastomys natalensis*), though recent research suggests viral presence in the reddish-white mastomys (*Mastomysery throleucus*) and "African wood mouse" (*Hylomyscus pamfi*) rodents as well [6,7].

In humans, Lassa virus infection occurs through the ingestion of contaminated food and/or water, or the inhalation of tainted aerosols from diseased rodents [8]. Person-to-person transmission can also occur through contact with infectious bodily fluids, putting healthcare professionals at greater risk [9]. According to the Centers for Disease Control and Prevention (CDC), over 300,000 new LASV infections occur each year, with around 5000 deaths [10] covering large endemic areas of West Africa putting 200 million people at risk of infection [11]. The usual case fatality rate is about 1%, although it can rise to 15–20% in hospitalized cases [8].

There are no vaccines against Lassa virus that have been authorized by the Food and Drug Administration (FDA). Currently, the only clinical therapy option is to utilize ribavirin off-label [12]. However, ribavirin

medication is costly, and it is only effective if started within the first six days of symptom onset [13]. LASV is classified as a class A pathogen because to the lack of vaccinations and effective treatments [14].The disease is endemic in several countries of the Africa. The objective of this paper is to delineate public health implications of Lassa fever that is as an emerging and re-emerging life threatening direct viral zoonosis.

2. Etiology

Lassa fever is a disseminated systemic primary viral infection that is caused by LASV, which belongs to the *Arenaviridae* family of single-stranded negative-sense RNA viruses [15]. Cryoelectron microscopy reveals that the virions have a pleomorphic form. Glycoprotein projections consisting of tetrameric complexes of the viral glycoproteins GP1 and GP2 adorn the virion envelope's surface [16]. LASV has a size range of 10 to 19 kilobases and two RNA species, the big and tiny units [17]. This virus contains two genomic sections, one large and one small, and four lineages have been found so far: Josiah (Sierra Leone), GA391 (Nigeria), LP (Nigeria), and strain AV [18].

3. Epidemiology

Lassa fever is an acute viral hemorrhagic fever that can occur as a sporadic case or may involve many persons in the form of an outbreak. Although Lassa fever has been recognized since the 1950s, the virus was not identified until 1969, when two missionary nurses died of the disease in the Nigerian town of Lassa. It is primarily found in West Africa and has the potential to kill tens of thousands of people. The virus persists in body fluids, including sperm, even after recovery [19]. The annual incidence of Lassa fever has been estimated at 300,000 infections and 5000–10,000 deaths in West African nations, such as Ghana, Guinea, Mali, Benin, Liberia, Sierra Leone, Togo, and Nigeria, however these statistics are most likely underestimates due to inadequate diagnosis and surveillance [20,21]. Except for the multimammate rat, no known bio-geographical or environmental discontinuities can clearly characterize the high-risk zones [22]. The expansion of Lassa virus infection outside of West Africa was fairly restricted as of 2013. Twenty to thirty instances had been reported in Europe, all of which were thought to be the result of infection spread by infected people [18].

4. Transmission

Multimammate rats (*Mastomys natalensis*), which breed frequently and are extensively spread over West, Central, and East Africa, are the natural hosts for Lassa virus [23]. The rats shed the virus in their excreta. Humans become infected after coming into contact with rats or eating raw rodent meat or rodent urine contaminated food and water [3,24]. The infection is usually spread through the respiratory or gastrointestinal systems after direct or indirect contact with animal excrement. The inhalation of microscopic infectious particles (aerosol) is thought to be the most common mode of infection. The infection can be contracted through broken skin or mucous membranes that have been exposed to infectious substances [3]. The disease has been proven to spread from person to person, posing a threat to healthcare personnel [18]. Despite the fact that the virus is still present in the sperm, the extent of sexual transmission remains uncertain [11]. Although no study has established the transmission by breast milk, the high level of viremia suggests its possible [25].

5. Clinical Spectrum

The incubation period of disease ranges from 5 to 21 days. In roughly 80% of persons who are infected, the condition is moderate or has no symptoms, whereas 20% have a severe multisystem disease [19]. Symptoms of Lassa fever usually occur 1–3 weeks after infection. When the condition is symptomatic, the onset is usually gradual, with fever, general weakness, and malaise as the first signs. Headache, sore throat, muscle discomfort, chest pain, nausea, vomiting, diarrhoea, cough, and stomach pain may occur within a few days. Swelling of the face, fluid in the lungs, bleeding from the mouth, nose, vaginal or gastrointestinal tract, and low blood pressure can all occur in severe cases. Hearing loss, encephalitis, and tremors are some of the neurological symptoms. Deafness affects around a quarter of those who survive the disease. During recuperation, temporary hair loss and gait disturbances are possible. Late in pregnancy, the condition is very severe, with maternal death and/or fetal loss happening in more than 80% of cases during the third trimester. If Lassa virus affects the liver, spleen, or kidneys, it can be fatal. Approximately two weeks after the onset of symptoms, death occurs owing to multi-organ failure [8,26].

6. Diagnosis

Different laboratory diagnostic tests are used to check for the presence of an infection and to assess its course and consequences. The presence of febrile infections in Africa that mimic Lassa fever, such as typhoid fever, is the most concerning issue, especially for nonspecific Lassa fever presentations [27]. Given the difficulties in identifying Lassa fever due to mutations, viral isolation in cell culture remains the “gold standard” for diagnosis [28]. Throat swabs, blood, urine, and cerebrospinal fluid specimens from individuals can also be cultured for the viral agent [3,29]. Rapid immunogenic testing is an appealing alternative to the technical requirements, especially in Lassa virus infected endemic areas [30]. Even if the specimens are not treated appropriately for viral isolation, antigen identification by ELISA is strong and reliable in fast fatal cases [31]. Due to its excellent specificity and sensitivity, real-time RT-PCR is a routinely used diagnostic tool for infectious pathogens and has become the gold standard clinically for Lassa fever detection [28,32].

7. Treatment

Ribavirin, an antiviral medicine, appears to be an effective treatment for Lassa fever when administered early in the course of clinical illness, but there is no evidence to support its use as a post-exposure prophylactic treatment [26]. When given intravenously rather than orally, ribavirin is about twice as effective, and if given within six days of the onset of disease, it can reduce fatalities by 90% [11]. Lassa fever infection has also been treated with intravenous interferon therapy [32]. Dehydration, oedema, hypotension, and impaired renal function are all common and therefore, fluid replenishment or blood transfusions must be carefully monitored [11].

8. Prevention and Control

To keep rodents out of homes, the prevention relies on maintaining good "community hygiene" [15]. Avoiding food, water, and environments contaminated by infected rodents can prevent the primary transmission of the Lassa virus from its rodent host to humans in endemic areas; however, due to the widespread distribution of these rodent hosts in Africa, complete control of these rodent reservoirs is impractical [33]. Other effective strategies include storing grain and other commodities in rodent-proof containers, disposing of rubbish far away from the home, keeping clean houses, and keeping cats. When caring for patients in health-care settings, regardless of their supposed diagnosis, workers should always use conventional infection prevention and control practices. Basic hand hygiene, respiratory hygiene, the use of personal protective equipment (to prevent splashes or other contact with infectious materials), safe injection techniques, and safe burial techniques are among them [26]. It is important that high security should be maintained in the laboratory [3].

There are no vaccines against LASV that have been authorized by the food and drug administration [12]. Several LASV vaccine candidates have shown efficacy in animal models, but only one has made it to the clinic [34]. GEO-LM01, offers a one-of-a-kind set of benefits for visitors and residents of LASV-endemic nations. As a vaccine candidate, GEO-LM01 offers a unique set of benefits that could help it fulfill the WHO's desired Target Product Profiles (TPP) for both non-emergency (Preventive Use) and emergency (Reactive/Outbreak Use) contexts [35]. Another viral platform, recombinant vesicular stomatitis virus (rVSV), has demonstrated some encouraging results as advanced vaccine candidates [36]. rVSV is a safe vaccine platform because it is engineered to lack the glycoprotein (G) gene, which is a recognized major viral pathogenic factor; and in its place, either the LASV GP or other gene(s) of pathogens like EBOV and Marburg virus (MARV) have been substituted [37]. The live attenuated mammarenavirus ML29 and vaccinia-vectored vaccine platforms are further promising vaccine candidates [38]. It is pertinent to mention that public should be educated about the mode of transmission, severity and preventive measures about Lassa fever which is a life threatening viral zoonosis [3].

9. Conclusion

Lassa fever is the most dangerous of all Arenavirus diseases, and most cases are reported from African countries. Several modes of disease transmission are recognized. Lassa fever infections are difficult to identify from other viral hemorrhagic fevers and more frequent febrile illnesses in clinical terms. The results of a clinical laboratory test are often inconclusive. In West African countries, RT-PCR assays that provide a conclusive diagnosis are not commonly available in the laboratories. Where it is available, it is prohibitively expensive for the poor people who live in endemic areas. The cost of ribavirin and barrier/isolated treatment is expensive once the diagnosis is made. Furthermore, Lassa fever is associated with a significant rate of mortality. It is also possible that the disease could be employed as a biological weapon. As a result, it is an infectious threat that must be prudently addressed. The person with skin injury should not be permitted to handle the rodents and their discharges. It is imperative to impart health education to the public about the mode of transmission, severity of disease, and preventive measures. It is emphasized that attempt should be made to develop the safe, potent and low cost vaccine that can be widely employed to immunize the susceptible people.

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Contribution of Authors

All the authors contributed equally. They read the final version, and approved it for the publication.

Conflict of Interest

The authors declare that they do not have conflict of interest.

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