

Lassa Fever: A Comprehensive Review

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Abstract: *Lassa fever is an acute viral hemorrhagic illness of 2-21 days duration that occurs in West Africa. The Lassa virus is transmitted to humans via contact with food or household items contaminated with rodent urine or faeces. Person-to-person infections and laboratory transmission can also occur, particularly in hospitals lacking adequate infection prevention and control measures. Lassa fever is known to be endemic in Benin, Ghana, Guinea, Liberia, Mali, Sierra Leone, and Nigeria, but probably exists in other West African countries as well. The overall case-fatality rate is 1%. Observed case-fatality rate among patients hospitalized with severe cases of Lassa fever is 15%. Early supportive care with rehydration and symptomatic treatment improves survival.*

Keywords: Lassa fever, viral hemorrhagic fever, infection

1. Introduction

Lassa fever is also known as Lassa hemorrhagic fever (LHF), is a type of viral hemorrhagic fever caused by the Lassa virus. Many of those infected by the virus do not develop symptoms. When symptoms occur they typically include fever, weakness, headaches, vomiting, and muscle pains. Less commonly there may be bleeding from the mouth or gastrointestinal tract. The risk of death once infected is about one percent and frequently occurs within two weeks of the onset of symptoms. Among those who survive about a quarter have hearing loss, which improves within three months in about half of these cases.¹ The disease is usually initially spread to people via contact with the urine or feces of an infected multi mammate mouse. Spread can then occur via direct contact between people. Diagnosis based on symptoms is difficult. Confirmation is by laboratory testing to detect the virus's RNA, antibodies for the virus, or the virus itself in cell culture. Other conditions that may present similarly include Ebola, malaria, typhoid fever, and yellow fever. The Lassa virus is a member of the Arenaviridae family of viruses. There is no vaccine.² Prevention requires isolating those who are infected and decreasing contact with the mice. Other efforts to control the spread of disease include having a cat to hunt vermin, and storing food in sealed containers. Treatment is directed at addressing dehydration and improving symptoms. The antiviral medication ribavirin has been recommended,¹ but evidence to support its use is weak.³ Descriptions of the disease date from the 1950s. The virus was first described in 1969 from a case in the town of Lassa, in Borno State, Nigeria. Lassa fever is relatively common in West Africa including the countries of Nigeria, Liberia, Sierra Leone, Guinea, and Ghana. There are about 300,000 to 500,000 cases which result in 5,000 deaths a year.¹

1.1 History

The disease was identified in Nigeria in 1969. It is named after the town Lassa in which it was discovered.⁴ A prominent expert in the disease, Aniru Conteh, died from the disease.⁵

1.2 Epidemiology

There are about 300,000 to 500,000 cases which result in 5,000 deaths a year.⁶ One estimate places the number as high as 3 million cases per year.⁴ Estimates of Lassa fever are complicated by the lack of easy-available diagnosis, limited public health surveillance infrastructure, and high clustering of incidence near high intensity sampling.⁷

1.3 Geography

Lassa high risk areas are near the western and eastern extremes of West Africa. As of 2018, the Lassa belt includes Guinea, Nigeria, Sierra Leone and Liberia.⁸ As of 2003, 10-16% of people in Sierra Leone and Liberia admitted to hospital had the virus.⁹ The case fatality rate for those who are hospitalized for the disease is about 15-20%. Research showed a twofold increase risk of infection for those living in close proximity to someone with infection symptoms within the last year. The high risk areas cannot be well defined by any known bio geographical or environmental breaks except for the multimammate rat, particularly Guinea (Kindia, Faranah and Nzerekore regions), Liberia (mostly in Lofa, Bong, and Nimba counties), Nigeria (everywhere) and Sierra Leone (typically from Kenema and Kailahun districts). It is less common in the Central African Republic, Mali, Senegal and other nearby countries, and less common yet in Ghana and the Democratic Republic of the Congo. Benin had its first confirmed cases in 2014, and Togo had its first confirmed cases in 2016.¹⁰

1.4 2018 outbreak

An outbreak of Lassa fever occurred in Nigeria during 2018 and spread to 18 of the country's states; it was the largest outbreak of Lassa recorded.¹¹ As of February 25, 2018, there were 1081 suspected cases and 90 reported deaths; 317 of the cases and 72 deaths were confirmed as Lassa.¹²

Lassa virus

GENUS: ARENAVIRUS

FAMILY: ARENAVIRIDAE

Name derived from the arenosus (Latin "sandy") describing appearance of virions on examination by electron microscopy. Enveloped virus, round or pleomorphic, 50-300nm in diameter. Single stranded genome divided into 2

RNA segments small (3.5kb), large (7.1kb). 2 genes on same segments arranged in unique "ambisense" orientation encoding 5 proteins.

Inactivated by heating to 56 degree centigrade, pH <5.5 or >8.5, UV/gamma irradiation, detergents.

Rodent reservoir

- Mastomys species complex
- Taxonomy is still unclear
- M. huberti*: more common in peridomestic habitat.
- M. erythroleucus*: more common in brush habitat.
- The dissemination of the infection can be assessed by prevalence of antibodies to the virus in populations
 - Sierra Leone: 8-52%
 - Guinea: 4-55%
 - Nigeria: 21%

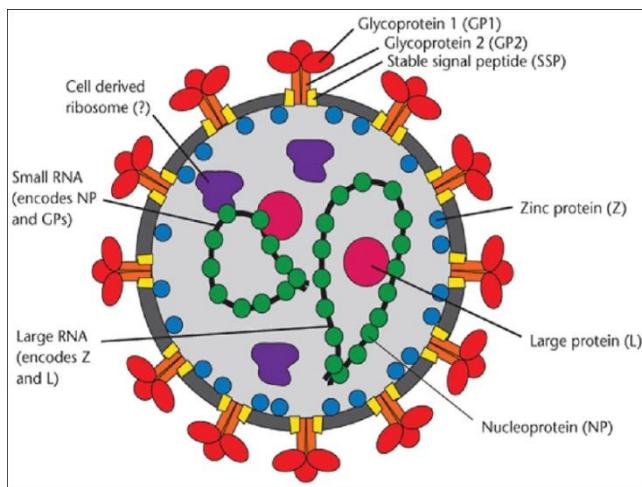


Figure 1: Lassa virus

1) Transmission

Humans usually become infected with Lassa virus from exposure to urine or faeces of infected Mastomys rats. Lassa virus may also be spread between humans through direct contact with the blood, urine, faeces, or other bodily secretions of a person infected with Lassa fever. There is no epidemiological evidence supporting airborne spread between humans. Person-to-person transmission occurs in both community and health-care settings, where the virus may be spread by contaminated medical equipment, such as re-used needles. Sexual transmission of Lassa virus has been reported. Lassa fever occurs in all age groups and both sexes. Persons at greatest risk are those living in rural areas where Mastomys are usually found, especially in communities with poor sanitation or crowded living conditions. Health workers are at risk if caring for Lassa fever patients in the absence of proper barrier nursing and infection prevention and control practices.¹³

2) Sign and symptoms

- Onset of symptoms is typically 7 to 21 days after exposure. In 80% of those who are infected little or no symptoms occur. These mild symptoms may include fever, tiredness, weakness, and headache.¹⁴
- Protein may be noted in the urine. Shock, seizures, tremor, disorientation, and coma may be seen in the later stages. Deafness occurs in 25% of patients who survive the disease. In half of these cases, hearing returns

partially after 1–3 months. Transient hair loss and gait disturbance may occur during recovery.¹⁴

- In 20% of people more severe symptoms such as bleeding gums, breathing problems, vomiting, chest pain, or dangerously low blood pressure may occur. Long term complications may include hearing loss. In those who are pregnant, miscarriage may occur in 95%. In cases in which death occurs, this typically occurs within 14 days of onset.¹⁴
- About 1% of all Lassa virus infections result in death. Approximately 15%-20% of those who have required hospitalization for Lassa fever die. The risk of death is greater in those who are pregnant. A "Swollen baby syndrome" may occur in newborns, infants and toddlers with pitting edema, abdominal distension and bleeding.¹⁵

In around 1 percent of all cases, Lassa fever is fatal, and around 15 to 20 percent of all hospitalizations for the disease will end in death. Death can occur within 2 weeks after the onset of symptoms due to multiple organ failure. One of the most common complications of Lassa fever is hearing loss, which occurs in around 1 in 3 infections. This hearing loss varies in degree and is not necessarily related to the severity of the symptoms. Deafness caused by Lassa fever can be permanent and total. It is particularly dangerous for women in the third trimester of pregnancy. Spontaneous loss of pregnancy occurs in around 95 percent of pregnancies.

3) Diagnosis

Lassa fever is most often diagnosed by using enzyme-linked immunosorbent serologic assays (ELISA), which detect IgM and IgG antibodies as well as Lassa antigen. Reverse transcription-polymerase chain reaction (RT-PCR) can be used in the early stage of disease. The virus itself may be cultured in 7 to 10 days, but this procedure should only be done in a high containment laboratory with good laboratory practices. Immunohistochemistry, performed on formalin-fixed tissue specimens, can be used to make a post-mortem diagnosis.

4) Treatment

Treatment is directed at addressing dehydration and improving symptoms.¹ All persons suspected of Lassa fever infection should be admitted to isolation facilities and their body fluids and excreta properly disposed of.

- Medications:-** The antiviral medication ribavirin has been recommended,¹ but evidence to support its use is weak. Some evidence has found that it may worsen outcomes in certain cases. Fluid replacement, blood transfusions, and medication for low blood pressure may be required. Intravenous interferon therapy has also been used.³
- Pregnancy:-** When Lassa fever infects pregnant women late in their third trimester, inducing delivery is necessary for the mother to have a good chance of survival. This is because the virus has an affinity for the placenta and other highly vascular tissues. The fetus has only a one in ten chance of survival no matter what course of action is taken; hence, the focus is always on saving the life of the mother.¹⁶ Following delivery, women should receive the same treatment as other people with Lassa fever.

5) Prevention

- Prevention of Lassa fever relies on promoting good “community hygiene” to discourage rodents from entering homes. Effective measures include storing grain and other foodstuffs in rodent-proof containers, disposing of garbage far from the home, maintaining clean households and keeping cats. Because *Mastomys* are so abundant in endemic areas, it is not possible to completely eliminate them from the environment. Family members should always be careful to avoid contact with blood and body fluids while caring for sick persons.
- Control of the *Mastomys* rodent population is impractical, so measures focus on keeping rodents out of homes and food supplies, encouraging effective personal hygiene, storing grain and other foodstuffs in rodent-proof containers, and disposing of garbage far from the home to help sustain clean households.
- Gloves, masks, laboratory coats, and goggles are advised while in contact with an infected person, to avoid contact with blood and body fluids. These issues in many countries are monitored by a department of public health. In less developed countries, these types of organizations may not have the necessary means to effectively control outbreaks.
- **Vaccine:**-There is no vaccine for humans as of 2019.¹⁷ Researchers at the United States Army Medical Research Institute of Infectious Diseases facility had a promising vaccine candidate in 2002. They have developed a replication-competent vaccine against Lassa virus based on recombinant vesicular stomatitis virus vectors expressing the Lassa virus glycoprotein. After a single intramuscular injection, test primates have survived lethal challenge, while showing no clinical symptoms.¹⁸

6) Prognosis

- About 15–20% of hospitalized people with Lassa fever will die from the illness. The overall case fatality rate is estimated to be 1%, but during epidemics, mortality can climb as high as 50%. The mortality rate is greater than 80% when it occurs in pregnant women during their third trimester; fetal death also occurs in nearly all those cases. Abortion decreases the risk of death to the mother.¹⁹ Some survivors experience lasting effects of the disease, and can include partial or complete deafness.¹
- Because of treatment with ribavirin, fatality rates have declined.

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