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Epidemiology and Comprehensive Review on the Myth and Facts of Lassa Fever Transmission

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ABSTRACT

Lassa fever (LF) is a hemorrhagic disease that is common throughout West Africa. It is mostly caused by unsanitary conditions and inadequate rat control, particularly in rural areas. Many people who contract the virus do not show any symptoms. When symptoms appear, they usually include headaches, weakness and fever. Flu-like symptoms, such as fever, lethargy and sickness, typically start first. Mastomys natalensis, commonly referred to as the multimammate mouse, serves as the virus' main host. Mice that are infected are virus carriers. The Lassa virus is the cause of Lassa fever in humans. Humans can also contract Lassa fever by eating food tainted with an infected mouse's excrement, urine or blood, among other things. Treatment is directed at addressing dehydration and improving symptoms. Ribavirin is currently used in treating individuals with cases of Lassa fever, as well as for post-exposure prophylaxis. When treating infected patients, health professionals are also at high risk of contracting the infection, especially if they do not follow infection prevention and control protocols to stop the nosocomial transmission of the Lassa virus. Therefore, with accurate information and appropriate measures, the impact of Lassa fever can be significantly reduced. Hence, increasing awareness and education about Lassa fever has been advocated for its prevention and control.

KEYWORDS

Lassa virus, *Mastomys natalensis*, viral haemorrhagic, Arenaviridae, Lassa fever

INTRODUCTION

A form of viral haemorrhagic fever brought on by the Lassa virus is called Lassa fever, often referred to as Lassa haemorrhagic fever. Many people who contract the virus do not show any symptoms. Symptoms include fever, weakness, headaches, nausea and sore muscles when they manifest. Initial symptoms typically include fever, malaise, cough, sore throat, intense headache, chest and abdominal pain, vomiting,

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and diarrhea. Later on, mucosal opening bleeding, severe haemorrhagic fever, facial edema and multi-organ dysfunction may occur, which may ultimately result in death[1]. Less frequently, there could be oral or gastrointestinal bleeding. Once infected, there is a one percent chance of mortality, which usually happens within two weeks of the commencement of symptoms. About 25% of those who survive have hearing loss, which in about half of these cases gets better in three months[2].

The Lassa virus (LV) causes Lassa fever in humans[1,3,4]. According to Kelly *et al*.[5], it is a single-stranded RNA virus that is a member of the Arenaviridae family. *Mastomys natalensis* is the virus' principal host[4,5]. Named after the multimammate mouse as well. Although asymptomatic, infected mice are carriers of the Lassa virus, which they can release into the environment through exposed blood vessels, urine, faeces, saliva and respiratory secretions[6].

Humans can contract Lassa fever by eating food contaminated with the urine, blood or faeces of an infected mouse or by coming into close contact with bodily fluids of an infected individual[7]. Eating rats that have the infection is another way that it might spread. Owing to the stability of the Arenavirus, infections in non-human primates by the aerosol route have been reported[6]. Six to twenty-one days after being exposed to the virus, infection may ensue[7]. Ninety percent of pregnant women experience foetal infection and/or foetal loss[8]. According to Olayemi *et al*.[4], Lassa fever can result in deafness in 25% of recovered cases and death in fourteen days for fatal cases.

Usually, the disease is first transmitted to humans through contact with an infected multimammate mouse's urine or faeces. Direct human contact is then one way that spread can happen[2]. Based on symptoms, diagnosis is challenging. Laboratory testing to identify the virus's RNA, antibodies against it, or the virus itself in cell culture is the method of confirmation[2]. Other illnesses including yellow fever, typhoid fever, malaria and Ebola can all manifest similarly. According to Asogun *et al*.[2], the Lassa virus belongs to the Arenaviridae family of viruses.

A vaccination does not exist[1]. Reducing interaction with the mice and isolating infected individuals are necessary for prevention[2]. Keeping a cat to hunt rodents and storing food in sealed containers are two further methods to stop the spread of illness. The goal of treatment is to alleviate symptoms and correct dehydration[1,2]. Although there is little evidence to support the use of the antiviral drug ribavirin, it has been advised[9,10].

The illness was first described in the 1950s. A case in the Nigerian Borno State Town of Lassa led to the first description of the virus in 1969[11]. In West Africa, which includes Nigeria, Liberia, Sierra Leone, Guinea and Ghana, Lassa fever is comparatively widespread[11]. A yearly total of between 300,000 to 500,000 cases lead to 5,000 fatalities[2, 12]. Lassa fever, which can manifest itself in both epidemic and sporadic forms, has been a recurring health problem in Nigeria. According to recent studies, there is an increasing tendency in the frequency of these outbreaks and their nationwide spread[13]. This study is evaluated to clarify the facts, myths and misconceptions surrounding the transmission of lassa fever.

Epidemiology of lassa fever: Every year, between 300,000 and 500,000 instances lead to 5,000 fatalities[12]. According to one prediction, there might be up to 3 million instances year[14]. The lack of an easily accessible diagnosis, the inadequate infrastructure for public health surveillance and the high incidence clustering around high-intensity sampling make it difficult to estimate Lassa fever[15]. Females are 1.2 times more likely than males to get infected. The age range where infections are most common is 21-30 years old[16].

High-risk Lassa areas are located close to West Africa's Eastern and Western borders. According to Greenky *et al.*[17], Guinea, Nigeria, Sierra Leone and Liberia are all part of the Lassa belt as of 2018. According to Richmond[18], the virus was present in 10-16% of hospitalized patients in Sierra Leone and Liberia as of 2003. About 15-20% of patients who are hospitalized for the illness die from it. Living close to someone who has experienced infection symptoms in the past year has been linked to a twofold increase in infection risk, according to research[16].

Lassa had only very slowly expanded outside of West Africa as of 2013. There have been twenty to thirty cases reported in Europe, all of which were linked to importation through infected people[14]. Because the patients' symptoms were misinterpreted as carrying a risk, prompt identification and treatment were delayed in these cases discovered outside of West Africa, increasing the likelihood of fatalities[14]. Because there is no human-to-human transmission in hospital settings, imported cases have not shown up in larger epidemics outside of Africa. In 2003, there was an anomaly wherein a healthcare professional contracted the infection prior to exhibiting evident symptoms[14].

Nigeria outbreak data: Lassa fever is prevalent in Nigeria, where yearly outbreaks often peak in December-April, the dry season, after the *Mastomy* rat's reproductive cycle in May-June (29). Notably, Nigeria experienced its worst Lassa fever outbreaks to date during the years 2018-2020. Rising numbers of confirmed cases were reported by the nation during these years: 633 in 2018, 810 in 2019 and 1,189 in 2020. These cases affected 29 states out of 36 and between January, 2014 and June 6, 2020, there were 837 deaths (case-fatality ratio ranging between 3 and 27%) and 2,847 total confirmed laboratory cases[19]. From 13 states in 2014 to 29 states in 2020, the number of cases is rising annually. According to Gupta *et al.*[8], 36, 32 and 7% of Nigeria's confirmed cases are in the states of Ondo (36%), Edo (32%) and Ebonyi. If people are aware of the diseases, it can help to reduce the spread of infectious diseases. As a result, this will allow for an early diagnosis and presentation, which will result in the best possible treatment option[2,8].

- **2018 outbreak:** It was the biggest Lassa outbreak ever documented when it struck Nigeria in 2018 and expanded to eighteen of the nation's states[20]. As of February 25, 2018, there were 90 reported deaths and 1081 suspected cases. Of these, 317 cases and 72 deaths were verified to be Lassa-related, bringing the total number of documented cases in 2018 to 431[21]
- **2019 outbreak:** With 810 cases overall and 167 deaths in Nigeria in 2019, the 2019 had the highest case fatality rate (23.3%) recorded up to that point[21]
- **2020 outbreak:** Beginning in the second week of January, there was an outbreak. By the tenth week, there were 144 deaths and 855 cases overall, translating to a case fatality rate of 16.8%[14]
- **2021 outbreak:** The Nigeria Center for Disease Control (NCDC) was informed on December 8, 2021, that two individuals had perished from Lassa fever[14]
- **2022 outbreak:** The outbreak assumed a new shape between January 3 and January 30, 2022, with 211 laboratory-confirmed cases of Lassa fever, including 40 fatalities (case fatality ratio: 19%) reported cumulatively in 14 of the 36 states and the Federal Capital Territory of Nigeria[22]. A total of 132 deaths with a case fatality rate (CFR) of 19.1% have been reported from January to March; this is less than the CFR for the same period in 2021 (21.0%)[14,22]

Signs and symptoms of Lassa fever: Usually, symptoms appear seven to twenty-one days following exposure[23]. Few or no symptoms appear in 80% of infected individuals[17,23]. Fever, fatigue, weakness and headache are some of these minor symptoms that may be present[23]. More serious symptoms such breathing difficulties, vomiting, chest pain, bleeding gums or dangerously low blood pressure may occur in 20% of cases. One of the long-term issues could be hearing loss. The 95% of females who are capable of bearing children may experience miscarriage when they are pregnant[23]. Clinically, Lassa fever can be challenging to differentiate from other viral haemorrhagic fevers, such Ebola virus disease. According to McCormick *et al.*[24], pharyngitis, soreness below the sternum, extra protein in the urine and fever can all be combined to more accurately diagnose Lassa fever.

When a death does occur, it usually does so within 14 days of the beginning[23]. Death occurs in about 1% of cases of Lassa virus infection. As 15-20% of people with Lassa fever who needed to be hospitalized pass away. Pregnant women have a higher chance of dying[23]. Newborns, babies and toddlers with pitting edema, abdominal distension and bleeding may experience "swollen baby syndrome"[17]. When a death does occur, it usually does so within 14 days of the beginning[23].

Virology of Lassa fever: According to Bowen *et al*.[25], the Lassa virus is a single-stranded RNA virus that is a member of the Arenavirus family, which is known to infect rodents silently and persistently. Lassa virus is distinct from other members of the Arenavirus family because of its unusual and non-characteristic pathogenesis, genetics and serology. Additionally, the Lassa virus exhibits genetic diversity, which complicates the process of creating a vaccine against it. The Lassa virus has a smooth surface envelope with T-shaped spikes and integrated glycoproteins. Its diameter, which is spherical in shape, ranges from 70 to 150 nm. The Lassa virus is a single-stranded RNA virus that belongs to the Arenavirus family, which is known to silently and persistently infect rodents, according to Bowen *et al*.[25].

The genome of the Lassa virus is located in a nucleocapsid, which is a surface envelope that varies in length from 400 to 1300 nm[26]. There are at least four lineages of the Lassa virus; three of them have been identified in Nigeria, while a fourth has been linked to Guinea, Liberia and Sierra Leone[27].

Reservoir species of Lassa fever: The most common rodent species in Sub-Saharan Africa, the multimammate rat (*Mastomys natalensis*), serves as the main host for the Lassa virus. The reason why the multimammate rats have fewer babies during the rainy season, even though they are able to reproduce all year long, could be because flooding is more likely to occur during this season[28]. According to Fichet-Calvet and Rogers[29], the multimammate rat is the animal reservoir for the Lassa virus, but it does not contract the infection. According to reports, the Lassa virus can spread both horizontally and vertically in multimammate rats, with horizontal transmission happening more frequently than vertical transmission[30]. Additionally, there is growing evidence that the Lassa virus can employ the African wood mouse, *Hylomyscus pamfi* and the Guinea multimammate mouse, *Mastomys erythroleucus*, as reservoir hosts[31]. In rural areas, multimammate rats are more common[30,32].

Myth and facts of Lassa fever transmission

Transmission/spread of Lassa fever: For the whole of its life, the multimammate rat that has contracted the Lassa virus may excrete and urinate the virus[33]. The Lassa virus is more likely to spread from the animal reservoir to the human host due to a variety of intricate interactions between humans and the environment[30]. For example, the risk of contracting the Lassa virus has seasonal variations in tropical West Africa, where hospitalized cases of Lassa fever peak during the dry season[34].

Multi-mammate rats have a habitat that is more suited for reproducing during the dry season since less rainfall is associated with a lower likelihood of flooding. According to Gibb *et al*.[30], zoonotic spill overs are hypothesized to happen when people come into contact with rodent urine and/or excreta through contaminated food or breathe in aerosols from dried urine or faeces. It is also possible for the virus to spread from person to person, especially in rural health institutions where medical staff members may come into touch with an infected person's blood, pharyngeal secretions or urine[33].

Furthermore, as the Lassa virus can linger in semen for up to three months following infection, there have also been examples of the virus spreading through sexual activity[35]. According to the Bell-Kareem and Smither[36], there is no proof that the Lassa virus may spread by air from sick to healthy people. Those who live in rural areas with a high concentration of multimammate rats are the ones most at risk of contracting the Lassa virus. When treating infected patients, health professionals are also at high risk of contracting the infection, especially if they do not follow infection prevention and control procedures to stop the nosocomial transmission of the Lassa virus[36].

Transmission of Lassa fever:

Facts: The multimammate rat (*Mastomys natalensis*), the virus's natural reservoir, is the main way that Lassa fever is spread[37]. The virus is excreted by these rodents in their urine and faeces, which contaminates surfaces, household goods and food. The most common way that human infection happens is through[33,37]:

- **Ingestion or inhalation:** Eating rat faeces, handling rat poop-infected items or breathing in small particles of contaminated stuff
- **Person-to-person transmission:** Person-to-person transmission can also happen when an infected person's blood, urine, faeces or other bodily fluids come into direct contact with you. However, this is less likely. In hospital environments, this is especially dangerous in the absence of appropriate safety precautions

Additional important information regarding the spread of Lassa fever is as follows[36,37]:

- **Incubation period:** The time frame for incubation varies from 6 to 21 days. Usually starting slowly, fever, overall weakness and malaise are the first symptoms to appear
- **Geographical distribution:** Lassa fever is endemic in West African nations such as Guinea, Nigeria, Sierra Leone and Liberia; however, due to travel, cases have been documented in other regions of the world on occasion
- **Asymptomatic cases:** Eighty percent of infections with Lassa fever are mild or asymptomatic. Severe cases may cause organ failure, breathing difficulties and bleeding

Myths about Lassa fever transmission: Many myths and misconceptions regarding Lassa fever endure despite abundant scientific data, which frequently results in unwarranted alarm or on the other hand, insufficient preventive efforts.

- **Myth:** Lassa fever is spread through casual contact
  - **Fact:** Lassa fever cannot be transmitted by simple handshakes, hugs or proximity to an infected person. According to Mylne *et al.*[38], it necessitates close contact with infectious elements like bodily fluids
- **Myth:** Lassa fever is airborne
  - **Fact:** Typically, the Lassa virus cannot be transmitted through the air. The virus does not spread through the air like the flu or common cold, despite the possibility of infection from inhaling particles contaminated with rodent excreta[39]
- **Myth:** Only people in rural areas are at risk
  - **Fact:** Urban environments also carry some risk, even though rural areas with larger *Mastomys natalensis* prevalence are not immune. Because rodents can live in a variety of habitats, Lassa fever can happen in both urban and rural areas[29,39]
- **Myth:** Lassa fever is always fatal
  - **Fact:** Even while Lassa fever can be extremely dangerous and even deadly, particularly if left untreated, many patients with the right medical attention recover completely. The case-fatality rate is approximately 1% overall, although hospitalized patients with severe disease may have a higher risk[29,38]

Diagnosis of Lassa fever: Enzyme-linked immunosorbent serologic assays, which are helpful in identifying IgM and IgG antibodies as well as the Lassa antigen, can be used to diagnose Lassa fever. However, Reverse Transcription-Polymerase Chain Reaction (RT-PCR) is the most popular and reliable method of virus detection. Immunohistochemistry can also be used for postmortem diagnosis when done on tissue samples that have been formalin-fixed[40]. Lassa fever has also been diagnosed in laboratories using antigen detection assays and virus isolation through cell culture[36].

Treatment of Lassa fever: The goals of treatment are to reduce dehydration and alleviate symptoms[2]. Nowadays, ribavirin is utilized for post-exposure prevention and the treatment of Lassa fever cases in individuals[26,41].

- **Medications:** Although there is little evidence to support the use of the antiviral drug ribavirin, it has been advised[2,15,22]. According to certain data, in some circumstances it might make things worse[15]. It might be necessary to administer blood transfusions, low blood pressure medication and fluid replenishment. There has also been usage of intravenous interferon therapy[42]
- **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[43]. 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[43]

Prevention of Lassa fever: Since it is impossible to control the *Mastomys* rodent population, efforts are directed toward preventing rodents from entering buildings and food supplies, promoting good personal hygiene, storing grains and other foods in rodent-proof containers and disposing of trash far from homes in order to maintain clean living spaces. When interacting with an infected person, it is recommended to wear gloves, masks, lab coats and goggles to prevent coming into touch with bodily fluids such blood[44]. The public health departments of many nations keep an eye on these matters. These kinds of groups might not have the resources needed in less developed nations to successfully contain outbreaks[44].

- **Vaccine:** As of 2023, there is no human vaccine[45]. In 2002, scientists at the US Army Medical Research Institute of Infectious Diseases facility discovered a potentially effective vaccine candidate[36]. Based on recombinant vesicular stomatitis virus vectors expressing the Lassa virus glycoprotein, they have created a replication-competent vaccine against the Lassa virus. Test primates have shown no clinical signs and survived lethal challenges after a single intramuscular injection[44,45].

Current Lassa fever trends: The number of suspected and confirmed cases of Lassa fever infections has increased during the last ten years. The reason for these increases is that instead of learning about Lassa fever from books and academic articles, people are now learning about it via real Lassa fever case reports found in disease surveillance reports[30]. In areas where the Lassa virus is endemic, the frequency of Lassa fever cases has increased recently. This might be related to West African Lassa fever surveillance stepping up[30]. The increasing trend of probable Lassa fever cases in Nigeria from 430 in 2015 to 900, 700 and 1081 in 2016, 2017 and 2018, respectively, is a solid illustration of this[36].

It has been observed using ecological niche modelling that outbreaks of the Lassa virus infection are correlated with specific environmental variables (rainfall, human population density and rice yields)[29]. Climate projections for West Africa indicate an increase in temperature and rainfall, which is anticipated to increase the likelihood of multimammate rats thriving in the subregion and as a result, increase the risk of Lassa virus infection in humans[30]. Additionally, estimates of land use in West Africa have produced conflicting results on the impact of land use on the incidence of Lassa fever cases in the future.

On the one hand, it is anticipated that land use for large-scale agricultural and subsistence farming would become prevalent in the future. Due to farming operations bringing humans into closer contact with contaminated aerosols from infected multi-mammate rats, this may facilitate the spread of the Lassa virus[30]. On the other hand, other predictions suggest that a rise in commercial agriculture in West Africa in the future may lower the likelihood of contracting the Lassa virus. This is because mechanized farming will decrease the number of people who may have come into contact with the infected vector in its natural habitat, which will ultimately result in a decrease in Lassa virus infections[46].

Because Lassa fever is more contagious, researchers are also attempting to determine how much the increased number of cases is related to overall climate change and global warming. A plausible rationale could be that increased temperatures would encourage the growth of more crops, which would supply food for more multimammate rats to survive. Given that multimammate rats can grow exponentially at rates 10-20 times faster than those of humans, conducive environmental conditions would greatly increase the likelihood of Lassa virus infection in humans[47].

Furthermore, some populations from endemic places may be able to become resistant to the Lassa virus over time. Data from the Yoruba people in Nigeria, who appeared to have developed some level of genetic resistance to the Lassa virus in contrast to other endemic locations, has partially supported this theory[48].

Possible reduction solutions of Lassa fever: Community hygiene is one of the most effective ways to slow down the spread of Lassa fever in endemic areas[36]. The CDC recommends that humans can prevent infection with the Lassa virus by avoiding contact with multimammate rats in areas where the virus is endemic. They also recommend that food be stored in rodent-proof containers and that homes be kept clean to prevent rats from breeding. These actions are expected to lower the risk of human infection with the Lassa virus[40]. Moreover, it is best to prevent people from eating rodents because the Lassa virus can infect humans during the capture, catching, or cleaning of an infected mouse. Although deploying traps to capture multimammate rats could potentially decrease the quantity of animals serving as reservoirs for the Lassa virus, doing so is impractical due to the rodents' dispersed distribution throughout West Africa[40].

In addition, there are situations in which a Lassa virus-infected individual requires care. It is expedient to take preventive action to restrict the spread of the infection, according to the CDC[40]. Setting up biological containment conditions, donning protective gear (masks, gloves, gowns and goggles), properly sterilizing equipment and isolating infected people are a few steps that can be taken to stop the virus from spreading to unprotected people[40].

Additionally, there are cases where people who visit areas where Lassa fever is endemic bring the virus back to their own or other countries. Lassa fever testing must to be done as soon as possible on people who are coming home with feverish symptoms, particularly if they have been traveling from West Africa[36].

In order to prevent and limit the spread of Lassa fever, residents of endemic regions-especially those living in rural areas-should be informed about practical ways to lower the rodent population[40].

The Lassa virus, a member of the Arenaviridae family, which was discovered in 1969 in the Nigerian Town of Lassa, is the cause of Lassa fever, a viral haemorrhagic sickness. A number of West African Nations, including Sierra Leone, Liberia, Guinea and Nigeria, are endemic for this illness. Usually, symptoms appear seven to twenty-one days following exposure. The goals of treatment are to reduce dehydration and alleviate symptoms. Currently, ribavirin is used for post-exposure prophylaxis as well as the treatment of Lassa fever cases in individuals. Since it is impossible to control the *Mastomys* rodent population, efforts are directed toward preventing rodents from entering buildings and food supplies, promoting good personal hygiene, storing grain and other foods in rodent-proof containers and disposing of trash far from homes in order to maintain clean households. There are still many myths and misconceptions around Lassa fever, despite tremendous advancements in medical knowledge and public health awareness. Effective disease control requires an understanding of the true nature of Lassa fever, as well as its transmission, symptoms and prevention.

CONCLUSION AND RECOMMENDATION

Despite being a dangerous and possibly fatal illness, Lassa fever is frequently misunderstood, which can impede attempts to avoid and control it. To mitigate the spread of the virus, it is imperative to comprehend the genuine mechanisms of transmission, which are largely contact with rodent excreta and less frequently, direct contact with an infected person's bodily fluids. For the public health education and response plans, it is crucial to debunk misconceptions such as the notion that the disease can spread casually or by air and the understanding that both urban and rural people can be impacted. By providing precise information and taking the right actions, Lassa fever's effects can be greatly diminished.

So, it is suggested that:

- Launch educational initiatives to enlighten local populations on the actual routes of Lassa fever transmission
- Stressing the value of maintaining proper hygiene and avoiding contact with rodent excrement
- Including lessons on Lassa fever prevention in school curricula to start teaching kids about prevention at a young age
- Giving healthcare personnel thorough training on infection control, with a focus on the use of personal protective equipment (PPE) and close adherence to isolation measures

SIGNIFICANCE STATEMENT

Dispelling myths such as the belief in casual or airborne transmission and recognizing that the disease can affect both rural and urban populations is essential for public health education and response strategies. With accurate information and appropriate measures, the impact of Lassa fever can be significantly reduced. Numerous complex interactions occur between humans and the environment that make the Lassa virus more likely to crossover from the animal reservoir to the human host. Despite clear scientific evidence, various myths and misconceptions about Lassa fever persist, often leading to unnecessary panic or conversely, inadequate preventive measures.

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