LASSA FEVER RESURRGENCE: THE NIGERIA PERSPECTIVE

Abstract

Lassa fever (LF) is one of the chronic, zoonotic, viral haemorrhagic diseases (or fevers) caused Lassa virus, belonging to the family of arenaviruses. The Lassa virus was described in the year 1950s, but was not named until 1969. The first case of Lassa fever was recorded in Nigeria, there have been several outbreaks across other West African nations such as Sierra Leone, Togo, Benin Republic, Guinea, Liberia, Ghana, and Mali. Of all viral hemorrhagic fevers (VHF) exported to the Europe and America, Lassa fever ranks the highest. In light of the current resurgence of Lassa fever in Nigeria, Lassa fever cases in the country has risen to 857, with 167 deaths recorded from the disease between January and July 2022. Ondo has 30% of the confirmed cases, followed by Edo with 26% and Bauchi with 14%. Lassa fever is caused by Lassa virus which is a member of the virus family *Arenaviridae*, comprising of Lassa, Junin, Lujo, Guanarito, and Machupo, the *Filoviridae* comprising of Ebola and Marburg viruses, and the *Bunyaviridae* made up of RifyVaey Fever and Crimean Congo haemorrhagic fever. Animal to human transmission is caused by contact with droplets from Natal Multimammate rat or the African rat (*Mastomysnatalensis*), while human-to-human transmission occurs through contact with infected fluid from an infected person. The incubation period of lassa fever to range between 6 – 21 days and is accompanied with the clinical symptoms such as gradual slight fever, malaise and general weakness, followed by serious symptoms like abdominal, chest, and muscle pains, cough, headache, sore throat, nausea, shock, swelling of the face, diarrhea, and frequent vomiting. More severe cases result to bleeding and eventually death. It can be prevented by avoiding areas endemic with the host animal, observing proper hygiene, and the use of proper personal protective equipment for health workers. No specific treatment is available for Lassa fever infection, although ribavirin has been suggested to be effective when administered at the onset of infection.

Keywords: *Lassa fever, haemorrhagic, disease, Arenaviridae, Mastomysnatalensis, ribavirin.*

Introduction

Lassa fever (LF) is one of the chronic, zoonotic, viral haemorrhagic diseases (or fevers) caused Lassa virus, belonging to the family of arenaviruses [1-2]. A report by the World Health Organization (WHO) showed that the Lassa virus was described in the year 1950s, but was not named until 1969 [1]. The nomenclature *Lassa fever*was given to the disease after the town where the first case occurred in Lassa town ofBorno state, Nigeria [2]. A study conducted by Akpedeet al. [3] revealed that since the first case of Lassa fever was recorded in Nigeria, there have been several outbreaks across other West African nations [4] especially countries such as Sierra Leone, Togo, Benin Republic [5], Guinea [2], Liberia, Ghana, and Mali [1]. The WHO reported that Lassa fever is likely to exist in other West African Countries [1]. Kofman and team [6] reported in their study that of all viral hemorrhagic fevers (VHF)exported to the Europe and America, Lassa fever ranks the highest [6-7].

Africa Centers for Disease Control and Prevention [8] reported that an estimated 100,000 to 300,000 people in West Africa contract the Lassa virus each year, and 5,000 people die as a result. Another projection by Goeijenbier*et al.* [9] reported Lassa fever infection cases to stand at as high as 3 million cases within one year. In terms of geography, it was reported by David*et al*. [10] that areas with proximity to Western and Eastern African extremes are prone to high risk of Lassa fever. In Sierra Leone and Liberia, the virus was prevalent in 10–16% of patients admitted

to hospitals as of 2003 according to Richmond and Baglole [11]. The rate of case fatalities for patients hospitalized for the illness is said to be between 15% and 20%. According to studies, persons who live close to someone who has had infection symptoms during the past year are twice more likely to be infected.

A study conducted by Maxmen [12] and Beaubien [13] reported that the largest Lassa fever outbreak recorded occurred in Nigeria in 2018, which spread through 18 states of the nation. The WHO on report on Lassa fever Emergency [14] also revealed that there have been 1081 suspected cases and 90 fatalities reported from 1stJanuary to 25th February 2018 from 18 states (Anambra, Bauchi, Benue, Delta, Ebonyi, Edo, Ekite, Federal Capital Territory, Gombe, Imo, Kogi, Lagos, Nasarawa, Ondo, Osun, Plateau, Rivers, and Taraba). 72 deaths were alsorecorded during this time, making 317 cases classed as confirmed and eight as probable (the case fatality rate for confirmed and probable cases is 22%). It was reported that there are 2845 contacts total, spread throughout the 18 states [14]. Another article published on Lassa fever in Nigeria for the year 2022 reported that from January 3rd through 30th 2022, there were 211 Lassa fever cases confirmed in the laboratory of which 40 deaths were recorded, which is up to 19% case fatality ratio [15]. This event was reported across 14 of 36 states of Nigeria, as well as the Federal Capital Territory.82% of confirmed cases are from three states: Ondo (63), Edo (57), and Bauchi (53). Benue (11), Ebonyi (5), Oyo (5), Taraba (5), Kogi (4), Enugu (2), Kaduna (2), Cross River (1), Delta (1), Katsina (1), and Plateau are the other states affected (1)[15]. According to WHO[3] [15], five cases among health professionals in two states, Edo (3) and Benue, have been recorded out of the 211 cases that have been verified in the lab (2).

In light of the current resurgence of Lassa fever in Nigeria, Premium Times Agency report as of July 30, 2022 [16] showed that Lassa fever cases in the country has risen to 857, with 167 deaths recorded from the disease between January and July 2022. According to a breakdown by Nigeria CDC, Ondo has 30% of the confirmed cases, followed by Edo with 26% and Bauchi with 14%. Further report showed that new cases were recorded from Edo and Ondo states which raised the number of confirmed cases from five between the 28th and the 29th week [16]. Conclusively, 24 States have been reported to at least record one confirmed case of Lassa fever across the 99 Local Government Areas. Additionally, 21 to 30 year-age range was found to be predominantly affected. On the basis of gender, the ratio of male-to-female infection rate stood at 10:8 [16-17] and the case fatalities recorded between the 1st week of the year (2022) and the 29th week was found to be less than those obtained for 2021. Further report cited a rise in the number of suspected cases for 2022 in comparison to the same period for 2021 and with respect to health professional exposure and infection, only one infection was recorded in Ondo state. According to WHO[3] [15], Lassa fever is endemic in Nigeria, and cases have been found to often reach their annual peak in the dry season which is between December–April. As a result, it is anticipated that there will be an increase in infections up until the conclusion of the dry season. It was recorded that there is a rise in the number of cases of Lassa fever after each season when compared to the previous epidemic and this was attributed to a reduction in the capacity to respond in surveillance and testing in the laboratory [15]. This research is an attempt to highlight the current issues on Lassa fever disease resurgence with respect to the Nigerian State.

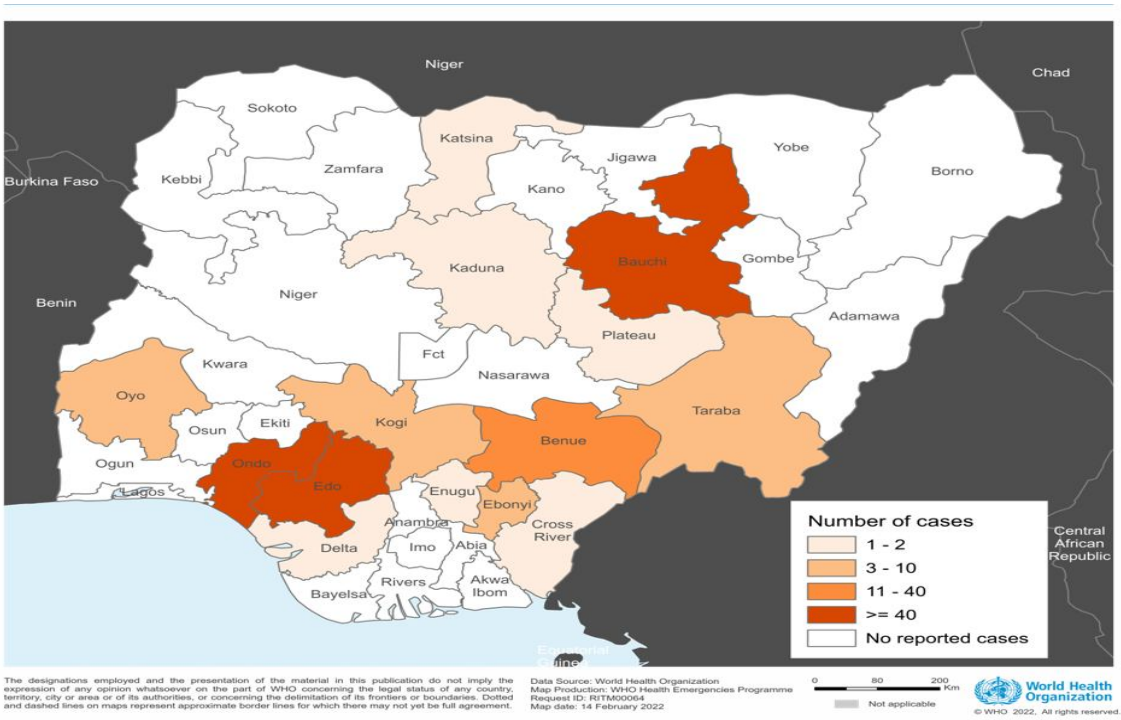

Fig. 1. Confirmed cases of Lassa fever by States reported in Nigeria from 3 – 30 January 2022 [15]

Cause and Transmission Mode

Cause

According to an article published by Viral Hemorrhagic Fever Consortium (VHFC) and Peterson *et al* [18-19], Lassa fever is caused by Lassa virus which is a member of the virus family *Arenaviridae*, comprising of Lassa, Junin, Lujo, Guanarito, and Machupo, the *Filoviridae* comprising of Ebola and Marburg viruses, and the *Bunyaviridae* made up of RifyVaey Fever and Crimean Congo haemorrhagic fever. Peterson et al. [19] further stated that these group of viruses are negatively sensed and are RNA viruses. A research carried out by Goeijenbier*et al*. [20] revealed that four lineages of Lassa fever virus have been identified thus far: Josiah (Sierra Leone), GA391 (Nigeria), LP (Nigeria), and strain AV. It was also discovered that the virus possesses both a large and a small genome portion.

Further description of the viral structure showed that the Lassa virus particle is round, oval, or pleomorphic, with a diameter measuring 110 to 130 nm and enveloped [18].The viral polymerase and zinc binding protein are encoded by the large segment, while the structural proteins nucleoprotein and glycoprotein precursor are encoded by the small segment. The S segment is expressed at a substantially higher rate during infection compared to the L segment, which has a significantly lower expression level.

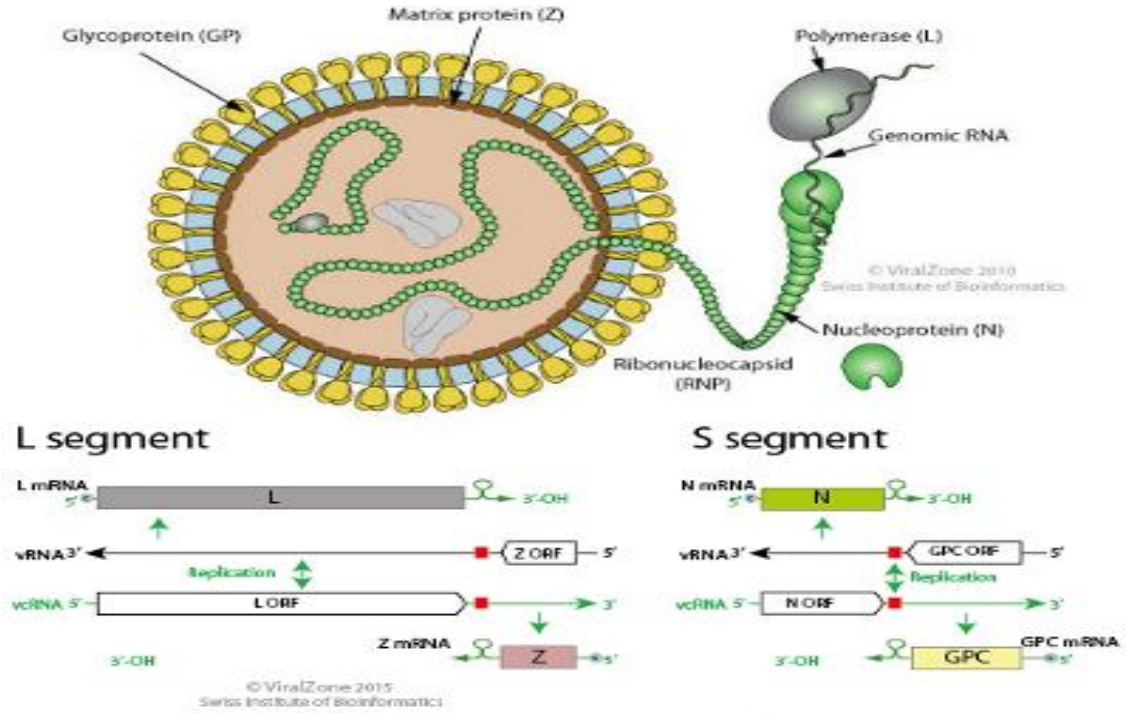

Fig. 2.Viral structure of Lassa virus [36]

Transmission Mode

The Natal Multimammate rat or the African rat(*Mastomysnatalensis*) have been particularly identified as the zoonotic host for Lassa fever [21-22]. Lassa fever is transmitted to humans via foods, or household items contaminated with droplets such as urine and faeces from infected *Mastomys rat's* [23]. According to the CDC's report, once the rats are infected with the virus, they are able to excrete it (Lassa virus) through their urine for a long duration, or throughout their life span [24]. According to the WHO[4] [23] and CDC [24] report, *Mastomys* are endemic to the Savannah and forests of West, Central, and Eastern Africa. They have also been found to reproduce in large numbers, giving them the ability for rapid colonization of their surrounding especially those of humans with food storage [24]. The ease of reproduction, ability to produce large number of offspring, and rapid colonization of their environment have all been found to contribute towards the quick and continuous zoonotictransmission of Lassa fever from *Mastomys* [24]. Animal to human transmission also occurs through direct contact with infected *Mastomys* [24], and consumption of the rats in in regions where they serve as food source [18]. Transmission has also been found to occur through broken skins, injuries, and inhalation of droplets in the form of aerosols or dustscontaining the virus from infected *Mastomys* rats [18,23-24].

Human-to-human transmission was reported by several studies to be very rare [18], but occurs both in community and healthcare scenario through direct contact with infected blood, secretions, tissues, contaminatedsharp such as needles, or excreta of persons infected with Lassa virus [18,23-24]. A study by David et al. [10] suggested that transmission via breast milk is possible, when consideration is given to the high level of viremia in the breast milk. This

assertion is yet to be verified. Transmission through seminal fluid has also been reported according to WHO[4] [23]. Human-to-human infection especially, nosocomial transmission has been attributed to the use of inappropriatepersonal protective equipment (PPE), or tending to infected patients without PPEs [18,24]. Close contact of caregivers and relatives of persons infected with Lassa fever is reported to be one of the causes of community infection [18]. According to VHFC researchers, zoonotic transmission accounts for over 95% of Lassa fever infection in persons infected with Lassa fever [18].

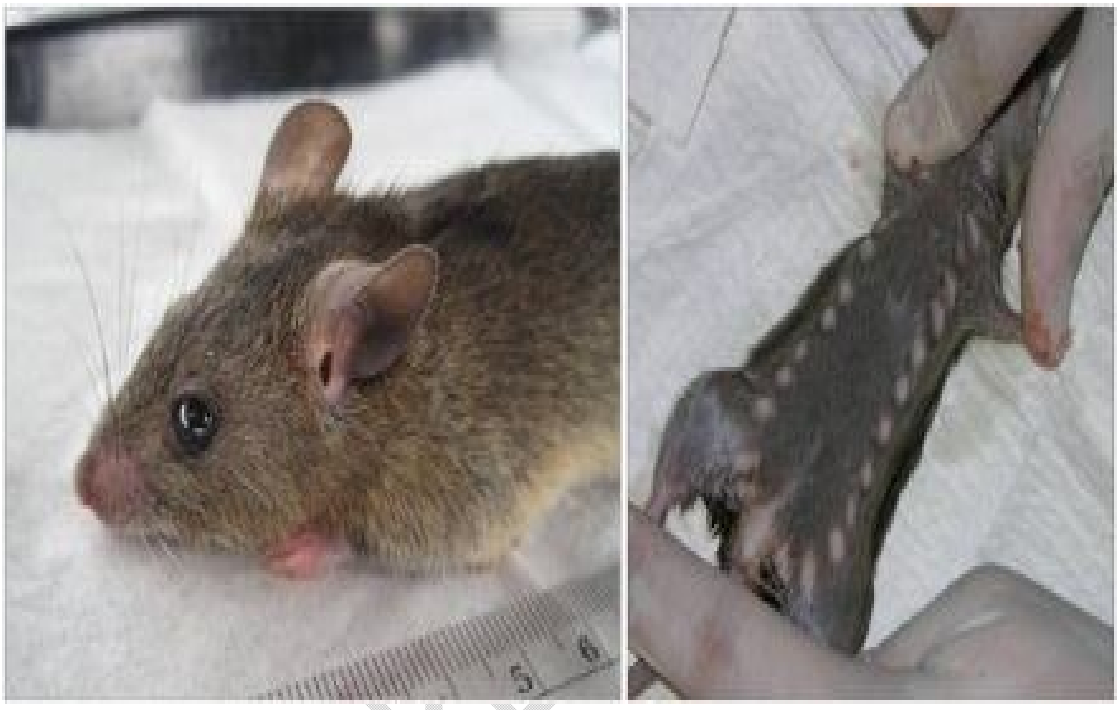

Fig. 3.Multimammate rat or the African rat (*Mastomysnatalensis)*[37]

Signs and symptoms

The WHO[4] [23] reported the incubation period of Lassa fever to range between 6 – 21 days. Some publications showed the range to stand between 1- 3 weeks [24] and 7 - 10 days [25] after contact with the virus [24]. The clinical symptoms which accompany symptomatic infection of Lassa fever occur gradually and begins with slight fever, malaise and general weakness [23-24]. Abdominal, chest, and muscle pains, cough, headache, sore throat, nausea, shock, swelling of the face, diarrhea, and frequent vomiting have been found to follow after the onset symptoms and are more serious[23-25]. This pattern was observed in 20% of persons infected with Lassa fever [24]. Neurological complications such as tremors, loss of hearing, and varying degrees of deafness have also been reported in about 25% of Lassa fever survivors [23-24]. According to WHO[4] [23], after 1-3 months, hearing returns partially in half of these individuals. During rehabilitation, temporary hair loss and gait instability may happen. Based on the CDC's report, typically 15%–20% of Lassa fever patients who are hospitalized pass away from the illness. Only 1% of Lassa virus infections cause death, nevertheless. Third-trimester pregnant women have very high mortality rates. With an estimated 80 - 95% death rate in fetuses of infected

expectant moms, spontaneous abortion is a major infection-related consequence [23-24]. In fatal cases, death is said to usually occur within 14 days of disease onset [23].

David *et el*. [10] in their work also noted that newborns, infants and toddlers with pitting edema, abdominal distension and bleeding which signs of "Swollen baby syndrome", may occur. Other symptoms reported in persons infected with Lassa virus revealed that sever cases of Lassa fever which results to multi-organ failure, is often accompanied with elevated number of protein metabolizing enzymes such as aspartate transaminase (AST) and alanine transaminase (ALT) [18]. Further research showed that a notable degree of hemolysis can be seen and patient's serum sample appearing brownish in coloration.

Diagnosis

According to several researches and that conducted by the WHO[4] [23], the symptoms of Lassa fever are not specific and varies because they appear like those of illnesses like typhoid, malaria, Ebola, Shigellosis, and yellow fever (illnesses which also present fever as symptoms). As a result, diagnosing Lassa fever clinically poses a challenge especially during the onset of the disease [19,23].Testing needed for a definitive diagnosis is only done in reference laboratories. Laboratory specimens are considered to be very hazardous; thus safe handling of the samples is advised. The tests employed in the laboratory for the definitive diagnosis of Lassa virus infections include: reverse transcriptase polymerase chain reaction (RT-PCR) assay, antibody enzyme-linked immunosorbent assay (ELISA), antigen detection tests, and virus isolation by cell culture [23-24].

Molecular Testing

Reverse transcriptase polymerase chain reaction (RT-PCR), loop-mediated isothermal amplification (LAMP), and other assays fall under molecular test types [26]. Molecular diagnosis is highly recommended because they are very sensitive in the detection of active infection of Lassa fever. They operate by detecting highly conserved areas of the Lassa virus genome.

Serological Testing

Serological diagnosis work by detecting IgM and IgG produced against Lassa virus antigens, and/or by directly capturing and detecting the Lassa virus itself [26]. Several studies reveal that at the acute stage of Lassa fever infection, all patients' IgM are not detectable, although IgM and antigen tests can be employed in active Lassa fever infection detection [27-29]. It was also reported in a research conducted by Fischer and Wohl [30], it was reported that in chronic infection cases, immunosuppression of both IgG and IgM can occur. IgG according to Sogoba*et al*. [31] is usually exclusively employed for surveillance, especially in endemic areas.It has been proven that LASV antigen testing is a reliable technique for identifying a current infection. Early antigen tests have revealed some heterogeneity in LASV lineage sensitivity, despite the fact that genetic sequence diversity and modest genetic changes normally have less of an impact on protein sequence [26]. Another study by Boisen*et al*. [32] showed that LASV NP antigen and anti-LASV IgM detection yielded 90% specificity and 88% sensitivity for early infection, which was sufficient to provide a diagnosis in 90% of PCR-positive patients.

Rapid Diagnosis

These are also known as rapid diagnostic tests (RDTs), are common to remote laboratories or healthcare facilities, and uses the same antibody/antigen capture agents as an ELISA but are packaged in a simplified lateral flow configuration, can be crucial for patient care and epidemic response. According to Boisen*et al*. [33-34], a RDT for Lassa virusthat utilizes a dipstick to sense Lassa virusnucleoprotein in fingerstick whole blood samples has been developed.When compared to its progenitor ELISA (94% sensitivity, 84% specificity; both related to quantitative PCR), the dipstick Lassa virusRDT for Lassa viruslineage IV (Josiah strain) performed well with respect to sensitivity (91% sensitivity, 86% specificity). Improvements to the assay utilizing a polyclonal method suggest greater pan-lineage antigen sensitivity, in contrast to the monoclonal capture agents used for this Lassa virusRDT, which shown decreased sensitivity to Lassa viruslineages II and III [32].

Risk factors

It has been reported by the CDC [24] that residents in, or travelers to endemic areas, such as Sierra Leone, Liberia, Guinea, and Nigeria, and are exposed to multimammate rats, are most at risk of contracting the Lassa virus. Other West African nations with *Mastomys* rodents may also have exposure risk. As long as precautions are taken and the right sterilizing techniques are applied, hospital employees are not at significant risk for infection.Sandraand Charles [25] reported that expectant mothers in their third trimester are most at risk for fatal complications and other significant issues. 95% of pregnancies result in stillbirth or fetal loss according to this research [25].

Prevention

Home

Lassa fever prevention according to the WHO[4] [23], depends on the promotion of proper hygiene within the community which prevents the entry of rats into homes. This approach minimizes zoonotic transmission as it limits contact between humans and Lassa virus reservoir [24]. Additionally, proper storage of food, garbage disposal, and tidying of the home to keep the rats away has been found to be an effective preventive measure. The application of biological and mechanical control methods through the use cats and trap setting is also suggested [23-24]. When caring for sick people, family members should always be cautious to prevent contact with blood and bodily fluids.*Mastomys* cannot be entirely eradicated from the environment since they are widely distributed in endemic regions [23-24].

Healthcare

Regardless of the patient's presumptive diagnosis, staffs in healthcare facilities are advised to always follow standard infection prevention and control protocols when providing treatment for patients. The use of personal protective equipment (PPE) (to prevent splashes or other contact with infected materials), patient’s isolation (quarantine), safe injection techniques, and safe burial techniques are a few examples of these [23-24].Healthcare professionals should wear gloves, a clean, non-sterile long-sleeved gown, and facial protection (a face shield or a medical mask and goggles) when in close proximity (within one meter) to Lassa fever patients (sterile gloves for some procedures) [23]. Adequate training on the right handling and processing of infected samples obtained from both humans and animals should be given to healthcare workers,

and all study should be carried out within very equipped laboratories under maximum biological containment guidelines [23].

Public

Awareness should be created regularly to the public on all available preventive measures including the elimination of rats in their surrounding and others such as proper food storage, clearing of bushes around living areas, and proper waste disposal [23]. Educating the general population to identify the signs and symptoms of Lassa fever infection and creating effective means for reporting any suspected case is also suggested [24].

Treatment

Supporting evidence regarding the availability of treatment for Lassa fever infection is weak and uncertain [23,35], however, ribavirin (an antiviral medication) has been recommended) [24]. According to the study of Eberhardt*et al*. [35], treatment with ribavirin could sometimes lead to worse consequences. The WHO[4] and the CDC [23-24] further noted that the ribavirin treatment was found to be effective against Lassa fever when it is administered at the early stage of the infection. As part of treatment, the CDC [24] recommends administering supportive care such as appropriate fluid and balancing of electrolyte, oxygenation and blood pressure, as well as treatment of any other complicating infections.

Recommendation

More study is highly recommended in finding out specific symptoms for identifying Lassa fever infection, as well as quick and exact effective diagnostic techniques, treatments, and vaccines for the illness.

Conclusion

Lassa fever (LF) is one of the chronic, zoonotic, viral haemorrhagic diseases (or fevers) caused Lassa virus, belonging to the family of arenaviruses. Having established in this study the economic importance of Lassa fever and its recent resurgence across the Nigerian society, there is a demand for more awareness, and strategizing by the relevant authorities to establish measures to limit the disease spread, minimize the reservoir within endemic states, and provision of treatment for those already infected.

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