Review Article

Formatted: Numbering: Continuous

LASSA FEVER IN NIGERIA

Abstract

According to World health organisation definition Lassa fever is a viral haemorrhagic fever that is transmitted to humans via contact with food or household items contaminated with rodent urine or faeces. Secondary transmission can also occur in human to human through direct contact with the blood, secretions, organs and other body fluids of infected persons which can more of nosocomial infection. This acute viral hemorrhagic fever caused by the Lassa virus was first described in 1969 in the town of Lassa, in Borno State, Nigeria. Lassa fever is named after the town (in the Yedseram River valley) in which the first cases were isolated in 1969, during a nosocomial outbreak at a local hospital. The Lassa fever is a member of the Aarenaviridiae virus family. Similar to Ebola, clinical cases of the disease had been known for over a decade but had not been connected with a viral pathogen. The main targets of the virus are antigen-presenting cells, (mainly dendritic cells) and endothelial cells. ELISA test for antigen and IgM antibodies gives 88% sensitivity and 90% specificity for the presence of the infection. High clustering of incidence near high intensity sampling make for an incomplete look at the impact of Lassa in Nigeria. All persons suspected of Lassa fever infection should be admitted to isolation facilities and their body fluids and excreta properly disposed of. Ribavirin is used for the treatment of Lassa fever. The best method to prevent Lassa fever is to keep rodents out of homes and food supplies, encouraging effective personal hygiene, storing grain and other foodstuffs in rodent-proof containers.

Key words: Lassa fever; haemorrhagic fever; arenaviridiae; ELISA test; IgM antibodies; Ribavirin

1.0 INTRODUCTION

1.1.0 LASSA FEVER OR LASSA HEMORRHAGIC FEVER (LHF)

This acute viral hemorrhagic fever caused by the Lassa virus was first described in 1969 in the town of Lassa, in Borno State, Nigeria. Lassa fever is named after the town (in the Yedseram River valley) in which the first cases were isolated in 1969, during a nosocomial outbreak at a local hospital. The Lassa fever is a member of the Arenaviridae~~arenaviridiae~~ virus family. Similar to Ebola, clinical cases of the disease had been known for over a decade but had not been connected with a viral pathogen (Dongo, *et al.*,2013).

Lassa fever is endemic in West African countries, and causes 300,000–500,000 cases annually, with approximately 5,000 deaths (WHO, 2016). Outbreaks of the disease have been observed in Nigeria, Liberia, Sierra Leone, Guinea, and the Central African Republic, but it is believed that human infections also exist in Democratic Republic of the Congo, Mali, and Senegal. The primary animal host of the Lassa virus is the Natal Multimammate Mouse (*Mastomys natalensis*), an animal indigenous to most of Sub-Saharan Africa (WHO, 2016). The virus is probably transmitted by contact with the feces or urine of animals accessing grain stores in residences. Given its high rate of incidence, Llassa fever has become a major problem in the African region. (PHE, 2016).

The primary animal host of the Lassa virus is the Natal Multimammate Mouse (*Mastomys natalensis*), an animal indigenous to most of Sub-Saharan Africa (Ayodeji *et al.*, 2016). The virus is probably transmitted by contact with the feces or urine of animals accessing grain stores in residences. (Guardian, 2018). Given its high rate of incidence, lassa fever has become a major problem in the African region (WHO, 2017).

1.1.1 LASSA VIRUS

Lassa virus (LASV) is an Old-World arenavirus that causes Lassa hemorrhagic fever, (Yun Nand Walker, 2012) a type of viral hemorrhagic fever (VHF) in human and non-human primates. Lassa virus is an emerging virus and a select agent, requiring Biosafety Level 4-equivalent containment. It is endemic in West African countries, especially Sierra Leone, the Republic of Guinea, Nigeria and Liberia, where the annual incidence of infection is between 300,000 and 500,000 cases, resulting in 5,000 deaths per year ~~(~~(Wikipedia, 2018)~~)~~. As of 2012 discoveries within the Mano River region of west Africa have expanded the endemic zone between the two

Comment [JAGH1]: The Lassa fever is not the virus. Lassa fever is the name of the disease caused by Lassa virus that belongs to Arenaviridae family.

Formatted: Highlight

Formatted: Highlight

Formatted: Font: Not Italic

Formatted: Font: Not Italic, Font color: Red

Formatted: Default Paragraph Font, Font: (Default) +Body, 11 pt, Font color: Red

Formatted: No underline, Font color: Red

Formatted: Default Paragraph Font, Font: (Default) +Body, 11 pt, Font color: Red

Formatted: No underline, Font color: Red

Formatted: Default Paragraph Font, Font: (Default) +Body, 11 pt, Font color: Red

Formatted: No underline, Font color: Red

Comment [JAGH2]: Delate this paragraph, it is repeated

Formatted: Font color: Red

Comment [JAGH3]: Change the source of information. Wikipedia is not a credible source.

known Lassa endemic regions, indicating that LASV is more widely distributed throughout the tropical wooded savannah ecozone in west Africa (Sogoba, *et al.*, 2012). There are no approved vaccines against Lassa fever for use in humans (Yun and Walker, 2012).

Formatted: Font: Not Italic, No underline, Font color: Auto

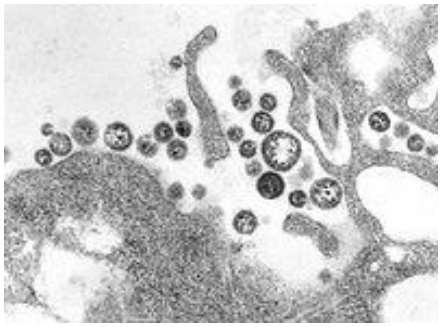

Plate 1: Lassa Virus as seen under scanning Electron Microscope

Source: CDC, 2014

Comment [JAGH4]: Where is the reference of this figure in the text?
Scale of nm?

1.1.2 LASSA VIRUS CLASSIFICATION

Group: Group V ((−) ssRNA)

Order: Unassigned

Family:Arenaviridae

Genus: Arenavirus

Species: Lassa virus

1.1.3 VIROLOGY

Structure and genome

Lassa viruses (Dyal and Fohner, 2018) are enveloped, single-stranded, bisegmented, ambisense RNA viruses. Their genome is contained in two RNA segments that code for two proteins each, one in each sense, for a total of four viral proteins (Yun and Walker, 2012).The large segment encodes a small zinc-binding protein (Z) that regulates transcription and replication,

(Fehling *et al.*, 2012) and the RNA polymerase (L). The small segment encodes the nucleoprotein (NP) and the surface glycoprotein precursor (GP, also known as the viral spike), which is proteolytically cleaved into the envelope glycoproteins GP1 and GP2 that bind to the alpha-dystroglycan receptor and mediate host cell entry (Wikipedia, 2018).

Lassa fever causes hemorrhagic fever frequently shown by immunosuppression. Lassa virus replicates very rapidly, and demonstrates temporal control in replication (Wikipedia, 2018). The first replication step is transcription of mRNA copies of the negative- or minus-sense genome. This ensures an adequate supply of viral proteins for subsequent steps of replication, as the NP and L proteins are translated from the mRNA. The positive- or plus-sense genome, then makes viral complementary RNA (vcRNA) copies of itself. The RNA copies are a template for producing negative-sense progeny, but mRNA is also synthesized from it. The mRNA synthesized from vcRNA are translated to make the GP and Z proteins. This temporal control allows the spike proteins to be produced last, and therefore, delay recognition by the host immune system.

Nucleotide studies of the genome have shown that Lassa has four lineages: three found in Nigeria and the fourth in Guinea, Liberia, and Sierra Leone. The Nigerian strains seem likely to have been ancestral to the others but additional work is required to confirm this (Dyal –and Fohner-, 2018).

Comment [JAGH5]: Move this cite to the final of sentence

Formatted: Font: Not Italic, No underline, Font color: Auto

Comment [JAGH6]: Change the source of information. Wikipedia is not a credible source.

Formatted: No underline, Font color: Auto, Highlight

Formatted: No underline, Font color: Auto, Highlight

Formatted: No underline, Font color: Auto, Highlight

Receptors

The Lassa virus enters the host cell by means of the cell-surface receptor the alpha-dystroglycan (alpha-DG), (Oppliger *et al.*, 2016) a versatile receptor for proteins of the extracellular matrix. It shares this receptor with the prototypic –Old-World arenavirus lymphocytic choriomeningitis virus. Receptor recognition depends on a specific sugar modification of alpha-DG~~alpha-dystroglycan~~ by a group of glycosyltransferases known as the LARGE proteins. Specific variants of the genes encoding these proteins appear to be under positive selection in West Africa where Lassa is endemic (Oldstone and Campbell, 2011). alpha-DG ~~Alpha-dystroglycan~~ is also used as a receptor by viruses of the New World clade C arenaviruses (Oliveros and Latino viruses). In contrast, the New World arenaviruses of clades A and B, which include the important viruses Machupo, Guanarito, Junin, and Sabia in addition to the non-pathogenic Amapari virus, use the transferrin receptor 1. A small aliphatic amino acid at the GP1 glycoprotein amino acid position 260 is required for high-affinity binding to alpha-DG. In addition, GP1 amino acid position 259 also appears to be important, since all arenaviruses showing high-affinity alpha-DG binding possess a bulky aromatic amino acid (tyrosine or phenylalanine) at this position.

Unlike most enveloped viruses which use clathrin coated pits for cellular entry and bind to their receptors in a pH dependent fashion, Lassa and lymphocytic choriomeningitis virus instead use an endocytotic pathway independent of clathrin, caveolin, dynamin and actin. Once within the cell the viruses are rapidly delivered to endosomes via vesicular trafficking albeit one that is largely independent of the small GTPases Rab5 and Rab7. On contact with the endosome pH-dependent membrane fusion occurs mediated by the envelope glycoprotein, which at the lower pH of the endosome binds the lysosome protein LAMP1 which results in membrane fusion and escape from the endosome.

Life cycle

The life cycle of Lassa virus is similar to the Old-World arenaviruses. Lassa virus enters the cell by the receptor-mediated endocytosis. Which endocytotic pathway is used is not known yet, but at least the cellular entry is sensitive to cholesterol depletion. It was reported that virus

Formatted: Font: Not Italic, No underline, Font color: Auto

Comment [JAGH7]: Add a diagram of replication

internalization is limited upon cholesterol depletion. The receptor used for cell entry is alpha-dystroglycan, a highly conserved and ubiquitously expressed cell surface receptor for extracellular matrix proteins. Dystroglycan, which is later cleaved into alpha-dystroglycan and beta-dystroglycan is originally expressed in most cells to mature tissues, and it provides molecular link between the ECM and the actin-based cytoskeleton (Moraz*et al.*, 2012). After virus enters the cell by alpha-dystroglycan mediated endocytosis, low-pH environment triggers pH-dependent membrane fusion and releases RNP (viral ribonucleoprotein) complex into the cytoplasm. Viral RNA is unpacked, and replication and transcription initiate in the cytoplasm (Moraz*et al.*, 2012). As the replication starts, both S and L RNA genomes synthesize the antigenomic S and L RNAs, and from the antigenomic RNAs, genomic S and L RNA are synthesized. Both genomic and antigenomic RNAs are needed for transcription and translation. S RNA encodes GP and NP (viral nucleocapsid protein) proteins, and L RNA encodes Z and L proteins. L protein most likely represents the viral RNA-dependent RNA polymerase (Bergeron, *et al.*, 2012). When the cell is infected by the virus, L polymerase is associated with the viral RNP and initiates the transcription of the genomic RNA. The 5' and 3' terminal 19 not viral promoter regions of both RNA segments are necessary for recognition and binding of the viral polymerase. The primary transcription first transcribes mRNAs from the genomic S and L RNAs, which code NP and L proteins, respectively. Transcription terminates at the stem-loop (SL) structure within the intergenomic region. Arenaviruses use a cap snatching strategy to gain the cap structures from the cellular mRNAs, and it is mediated by the endonuclease activity of the L polymerase and the cap binding activity of NP. Antigenomic RNA transcribes viral genes GPC and Z, encoded in genomic orientation, from S and L segments respectively. The antigenomic RNA also serves as the template for the replication (Yun and Walker, 2012). After translation of GPC, it is post translationally modified in the endoplasmic reticulum. GPC is cleaved into GP1 and GP2 at the later stage of the secretory pathway. It is reported the cellular protease SKI-1/S1P was responsible for the cleavage. Cleaved glycoproteins are incorporated into the virion envelope when the virus buds and release from the cell membrane (Bergeron et al., 2012).

1.2 PATHOGENESIS

Lassa fever is mostly caused by the Lassa virus. The symptoms include flu-like illness characterized by fever, general weakness, cough, sore throat, headache, and gastrointestinal manifestations. Hemorrhagic manifestations include vascular permeability (Yun and Walker, 2012). Upon entry, the Lassa virus infects almost every tissue in the human body. It starts with the mucosa, intestine, lungs and urinary system, and then progresses to the vascular system (CDC, 2016).

The main targets of the virus are antigen-presenting cells, mainly dendritic cells) and endothelial cells. In 2012 it was reported how Lassa virus nucleoprotein (NP) sabotages the host's innate immune system response. Generally, when a pathogen enters into a host, innate defense system recognizes the Pathogen-associated molecular patterns (PAMP) and activates an immune response. One of the mechanisms detects double stranded RNA (dsRNA), which is only synthesized by negative-sense viruses. In the cytoplasm, dsRNA receptors, such as RIG-I (retinoic acid-inducible gene I) and MDA-5 (melanoma differentiation associated gene 5), detect dsRNAs and initiate signaling pathways that translocate IRF-3 (interferon regulatory factor 3) and other transcription factors to the nucleus. Translocated transcription factors activate expression of interferons **α** and **β**, and this initiate adaptive immunity. NP encoded in Lassa virus is essential in viral replication and transcription, but it also suppresses host innate IFN response by inhibiting translocation of IRF-3. NP of Lassa virus is reported to have an exonuclease activity to only dsRNA (Hastie~~,~~ *et al.*, 2012). The NP dsRNA exonuclease activity counteracts IFN responses by digesting the PAMPs thus allowing the virus to evade host immune responses (Hastie *et al.*, 2012).

Lassa virus is zoonotic, is transmitted from animals ~~(i.e zoonotic)~~, in that it spreads to man from rodents, specifically multi-mammate rats (~~*Mastomys*~~*M. natalensis*). This is probably the most common rodent in equatorial Africa, ubiquitous in human households and eaten as a delicacy in some areas. In these rat's infection is in a persistent asymptomatic state. The virus is shed in their

excreta (urine and feces), which can be aerosolized. In fatal cases, Lassa fever is characterized by impaired or delayed cellular immunity leading to fulminant viremia (CDC, 2018).

Infection in humans typically occurs via exposure to animal excrement through the respiratory or gastrointestinal tracts. Inhalation of tiny particles of infective material (aerosol) is believed to be the most significant means of exposure. It is possible to acquire the infection through broken skin or mucous membranes that are directly exposed to infective material. Transmission from person to person has also been established, presenting a disease risk for healthcare workers. Frequency of transmission via sexual contact has not been established (NCBI, 2018).

1.3 VECTOR

The rat species *Mastomys*, in particular, *M. natalensis*. This is a consistent host reservoir for the Lassa virus because of congenital neonatal infection, which results in rats with long-lasting and/or lifelong infection (WHO,2017). Because of the mechanism of infection, there is no break in the natural chain from virus to host species. The rats themselves might show no symptoms of the disease, but they shed the virus freely in urine and droppings, and secrete the virus in their saliva.

Comment [JAGH8]: Is not clear. Change structure of sentence

Certain varieties of *Mastomys* often live in human homes, the virus is easily transmitted to humans. Transmission occurs via direct contact with rat urine, feces, and saliva; via contact with excretion- or secretion-infected materials; or via ingestion of excretion-contaminated food. Victims can also become infected via skin breaks, and via mucous membranes from aerosol transmission from dust-borne particles. In some areas, the rodents are used as a food source, thus providing additional exposure to the infected rat blood, as well as allowing ingestion of potentially contaminated meat. Laboratory workers become infected usually from contact with rodent saliva (WHO, 2017).

Plate 2: Mastomys *natalensis*, the natural reservoir of the Lassa fever virus

Source: CDC, 2018.

Comment [JAGH9]: Where is this figure cited in the text?

2.0 PREVALENCE

The dissemination of the infection can be assessed by prevalence of antibodies to the virus in populations of:

- Sierra Leone 8–52%
- Guinea 4–55%
- Nigeria approx. 29%(WHO,2018)

Lassa fever is a viral hemorrhagic fever in West Africa. (Asogun, *et al*, 2012). Studies show up to half a million cases of lassa fever per year in West Africa, with about 5,000 resulting in death. (Ehichioya*et al.*, 2012). Results Lassa virus was detected in 25 of 60 (42%) patients in northern and central Edo. (Preston R., 2002). The Lassa Virus affects adults and children alike; no matter your age you can be at risk for Lassa. (Ehichioya, 2012)

Comment [JAGH10]: this is very repetitive

Formatted: Font: Not Italic, No underline, Font color: Auto

Like other hemorrhagic fevers, Lassa fever can be transmitted directly from one human to another. It can be contracted by an airborne route or with direct contact with infected human blood, urine, or semen. Transmission through breast milk has also been observed (Tal, 2016).

2.1 SYMPTOMS OF LASSA FEVER

The incubation period of Lassa fever ranges from 6–21 days. The onset of the disease, when it is symptomatic, is usually gradual, starting with fever, general weakness, and malaise. After a few days, headache, sore throat, muscle pain, chest pain, nausea, vomiting, diarrhoea, cough, and abdominal pain may follow. In severe cases facial swelling, fluid in the lung cavity, bleeding from the mouth, nose, vagina or gastrointestinal tract and low blood pressure may develop.

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.

Death usually occurs within 14 days of onset in fatal cases. The disease is especially severe late in pregnancy, with maternal death and/or fetal loss occurring in more than 80% of cases during the third trimester (WHO, 2017).

2.2 TRANSMISSON

Lassa virus commonly spreads to humans from other animals, specifically the natal multimammate rat or African rat, also called the natal multimammate mouse (*M. ~~astomys~~natalensis*) (Richmond and Baglole 2011). This is probably the most common mouse in equatorial Africa, common in human households and eaten as a delicacy in some areas (Richmond and Baglole 2011).

The multimammate rat can quickly produce a large number of offspring, tends to colonize human settlements increasing the risk of rodent-human contact, and is found throughout the west, central and eastern parts of the African continent (Werner and Dietrich 2012). Once the rat has become a carrier, it will excrete the virus throughout the rest of its lifetime through feces and urine creating ample opportunity for exposure (Werner and Dietrich 2012). The virus is probably transmitted by contact with the feces or urine of animals accessing grain stores in residences (Richmond and Baglole 2011).

Individuals who are at a higher risk of contracting the infection are those who live in rural areas where *Mastromys* are discovered, and where sanitation isn't prevalent. Infection typically occurs by direct or indirect exposure to animal excrement through the respiratory or gastrointestinal tracts. Inhalation of tiny particles of infectious material (aerosol) is believed to be the most significant means of exposure. It is possible to acquire the infection through broken skin or mucous membranes that are directly exposed to infectious material. Transmission from person to person has been established, presenting a disease risk for healthcare workers. The virus is present in urine for between three and nine weeks after infection, and it can be transmitted in semen for up to three months after becoming infected (PHE, 2016).

Formatted: Font: Italic, No underline, Font color: Auto

No study has proven presence in breast milk, but the high level of viremia suggests it may be possible (David *et al.*, 2018).

2.3 DIAGNOSIS

There is a range of laboratory investigations that are performed to diagnose the disease and assess its course and complications. ELISA test for antigen and IgM antibodies gives 88%

sensitivity and 90% specificity for the presence of the infection. Other laboratory findings in Lassa fever include lymphopenia (low white blood cell count), thrombocytopenia (low platelets), and elevated aspartate aminotransferase (AST) levels in the blood (Dongo*et al., 2013*). Lassa fever can also be found in cerebrospinal fluid (Okokhere*et al.*, 2018). In West Africa, where Lassa is most prevalent, it is difficult for doctors to diagnose due to the absence of proper equipment to perform tests. (Asogun*etal, 2012).* In cases with abdominalpain, diagnoses in endemic countries are often made for other illnesses, such as appendicitis and intussusceptions, delaying treatment with Ribavirin. (Dongo*et al., 2013*)

2.4 PROGNOSIS

About 15–20% of hospitalized Lassa fever patients will die from the illness. The overall mortality 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 (CDC,2017). Some survivors experience lasting effects of the disease, and can include partial or complete deafness (WHO, 2017).

Because of treatment with ribavirin, fatality rates are continuing to decline (WHO, 2016).

Comment [JAGH11]: this sentence is lost, fix it

When Lassa fever infects pregnant women late in their third trimester, it is necessary to induce delivery for the mother to have a good chance of survival (Fisher-Hoch and McCormick, 2011).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 focus is always on saving the life of the mother. Following delivery, women should receive the same treatment as other Lassa fever patients (WHO, 2017).

3.0 EPIDEMIOLOGY

The study of the epidemiology of Lassa fever is complicated by a lengthy incubation period, which may be up to three weeks (Peterson *et al.*, 2013). Incubation periods as long as Lassa fever

may affect spatial clustering of the disease by limiting the understanding of the incidence and distribution of the disease. The spatial clustering for this disease is still in development as a lack of easy-available diagnosis, limited public health surveillance infrastructure, and high clustering of incidence near high intensity sampling make for an incomplete look at the impact of Lassa in this NIgeria (Peterson *et al.*, 2013). The number of people infected by Lassa range from 100,000 to three million a year, with up to 5,000 deaths per year in West Africa alone (GO *et al.*, 2013).

3.1 RECENT LASSA FEVER OUTBREAK IN SOUTHWEST NIGERIA

LAGOS STATE

The first occurrence was a 32-year-old pregnant lady with bleeding disorder who died after a stillbirth. Post-mortem examination was conducted before her Lassa fever status was eventually suspected and confirmed. No less than 100 different hospital workers exposed to this index case were monitored (Gaurdian, 2017). Resident doctor and one other health personnel were infected, isolated in hospital's ward and died (Gaurdian,2017).

OGUN STATE

A 20-year-old patient tested positive for the virus and was moved to one of the isolation centers set up by the state government. 66 persons who had contact with the victim were quarantined. (Thisday, 2017).

EKITI STATE

In January 2016, an 18-year-old student nurse, who was admitted with history of fever, headache and sore throat was suspected and confirmed. Throughout the outbreak Ekiti state recorded 10 cases (Aduayi*et al.*,2017).The 10 cases were detected from four LGAs across the state – Ado LGA (4), Ido-Osi LGA (3), Emure LGA (2), and Ikere LGA (1)(Aduayi et al.,2017).

ONDO STATE

Is one of the 3 states in Nigeria that carries the burden of Lassa Fever (WHO,2018). In January, 2013,21 cases were reported in Ose LG of Ondo state. There are 19 confirmed cases One person was recorded dead in Ose LG Area of Ondo State in January 2018. There was One death and 24 confirmed cases in different Local Governments Area of the state in January, 2018 (Premium Times, 2018). The number of deaths recorded later raised to 9 in February 2018 and number of suspected cases raised to 102 (Premium Times, 2018).The cases of this deadly disease were recorded in 8 Local Governments Area which are Akure south, AkureNorth, Akoko North East, Ondo West ,Ose, Owo, Akoko South East and Akoko South West (SaharaReporters,2018).

OYO STATE

In 2012 at Egbeda Local government, there were 2 cases of Lassa fever virus.One confirm and one suspected, both were male age 32 and 28.Number of death is 1 ,there is no linkage between the confirmed and suspected case(Adedire*etal*.,2014).

In 2016, aneight-month-old named Aishat was infected. It was confirmed at UCH Ibadan

(Adedire*etal*., 2014).

OSUN STATE

In 2017, a corpse was brought in from Lagos and was tested positive to Lassa fever. The relative of the corpse was placed on surveillance for 21days. Currently, there is no confirmed case of Lassa Fever outbreak anywhere in Osun State (Sunnewsonline, 2018).

3.2 TREATMENT

All persons suspected of Lassa fever infection should be admitted to isolation facilities and their body fluids and excreta properly disposed of. Early and aggressive treatment using Ribavirin was pioneered by Joe McCormick in 1979. After extensive testing, it was determined that early administration is critical to success. Additionally, Ribavirin is almost twice as effective when given intravenously as when taken by mouth (Fisher-Hoch and McCormick 2011). Ribavirin is a

prodrug which appears to interfere with viral replication by inhibiting RNA-dependent nucleic acid synthesis, although the precise mechanism of action is disputed (Crotty *et al.,* 2010). The drug is relatively inexpensive, but the cost of the drug is still very high for many of those in West African states. Fluid replacement, blood transfusion and fighting hypotension are usually required. Intravenous interferon therapy has also been used (Crotty *et al.,* 2010).

When Lassa fever infects pregnant women late in their third trimester, it is necessary to induce delivery for the mother to have a good chance of survival (Price *et al.*,2011). 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 focus is always on saving the life of the mother (Daso, 2017). Following delivery, women should receive the same treatment as other Lassa fever patients.Work on a vaccine is continuing, with multiple approaches showing positive results in animal trials (WHO, 2017).

3.3 PREVENTION

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.

Researchers at the United States Army Medical Research Institute of Infectious Diseases facility, where military biologists study infectious diseases, have a promising vaccine candidate (Preston, 2010). 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 (Geisbert*et al.,* 2011).

The use of standard precautions is recommended with all patients in a healthcare environment (WHO, 2014). This includes a minimum level of standard precautions for use with all people

regardless of their infection status, routine handwashing practices, safe handling and disposal of used needles and syringes, and intensifying standard precautions. It also includes VHF isolation precautions when needed (WHO, 2014).

Limited supplies and resources may prevent a health facility from using all the standard precautions all the time. However, health facilities should establish and maintain a basic, practical level of standard precautions that can be used routinely with patients in their health facility (WHO, 2014). This requires a source of clean water, routine handwashing before and after any contact with a person who has fever, and safe handling and disposal of sharp instruments and equipment (WHO, 2014).

Washing hands with soap and water eliminates microorganisms from the skin and hands. This provides some protection against transmission of Lassa fever and other diseases (WHO, 2014). This requires at least cake soap cut into small pieces, soap dishes with openings that allow water to drain away, running water or a bucket kept full with clean water, a bucket for collecting rinse water and a ladle for dipping, if running water is not available, and one-use towels (WHO, 2014).

The hand washing technique that is recommended is to place a piece of soap in the palm of one hand, wash the opposite hand and forearm, rub the surfaces vigorously for at least 10 seconds, move soap to the opposite hand and repeat, use clean water to rinse both hands and then the forearms, dry the hands and forearms with a clean one-use towel, or let rinsed hands and forearms air-dry (WHO, 2014). Reusable needles and syringes are not recommended. If reusable needles and syringes are used, clean, disinfect and sterilize them before reuse. Needles and syringes used with VHF patients require special care. Cleaning staff should wear two pairs of gloves when handling needles and syringes used with any patient with a known or suspected Lassa fever (WHO, 2014).

4.0 CONCLUSION

The Lassa fever outbreak provided a crucial opportunity to reveal challenges and improve preparedness for managing subsequent outbreaks. Nevertheless, close monitoring, active case search, contact tracing, laboratory support and disease awareness (both in community in general and specific training for health care workers) should continue (Aduayi *et al*., 2017).

REFERENCES

Adedire Elizabeth B., Gbolahan A., Nguku P., Usman A., Ogunniyi O., Gbadegesin Y. (2014). Outbreak of Lassa Fever in a Bakery: Investigation and Epidemiological Surveillance of Contact Persons, Ibadan Oyo State, Southwestern Nigeria. 16TH ICID Conference 2ND-5 TH April 2014 International Convention Centre Cape town South Africa.

Aduayi Victor Adovi, IbikunleOluwafunmilayo, Fashola Adebayo Matthew, Yusuf Musah ,Odu

Olusola1, Oluwafemi OmoniyiStephen,OlomojobiFolakemi,Ojo Simeon Olurotimi, Omole Ayotunde , Onwu Victor , Bamidele Oni (2017). Lassa Fever Outbreak in Southwestern Nigeria: The Ekiti State Response amidst Economic Recession Central African Journal of Public Health 2017; 3(2): 11-18

Asogun, D. A.; Adomeh, D. I.; Ehimuan, J. (2012). Molecular Diagnostics for Lassa Fever at Irrua Specialist Teaching Hospital, Nigeria: Lessons Learnt from Two Years of Laboratory Operation". PLoS Neglected Tropical Diseases. 6 (9): e1839.

Ayodeji Olayemi, Daniel Cadar, N'FalyMagassouba, AdeobaObadare, (2016). New Hosts of The Lassa Virus. Science Report, 6: 25280.

Bergeron E, Chakrabarti AK and Bird BH(2012). Reverse genetics recovery of Lujo virus and role of virus RNA secondary structures in efficient virus growth. Journal of Virology. 86:10759–10765.

Centre for Disease and Control and Prevention. (2016). Lassa Fever. Retrieved 2016-09-23.

Crotty S, Cameron C, Andino R (2002). Ribavirin's antiviral mechanism of action: Lethal Mutagenesis. Journal of Molecular Medicine. 80 (2): 86–95.

David Greenky, Barbara Knust, Eric J. Dziuban (2018). What Pediatricians Should Know About Lassa Virus. JAMA Pediatrician;172(5):407-408.

Dongo, A. E.; Kesieme, E. B.; Iyamu, C. E.; Okokhere, P. O.; Akhuemokhan, O. C.; Akpede, G. O. (2013). Lassa fever presenting as acute abdomen: a case series. Virology Journal. 10: 124

Dyal Jamie and Fohner Ben (2018). Lassa Virus. Stanford University Humans and Viruses Class of 2005, North Dakota, United State.

Ehichioya, D. U.; Asogun, D. A.; Ehimuan, J.; Okokhere, P. O.; Pahlmann, M.; Ölschläger, S.;

Formatted: No underline, Font color: Auto, Spanish (Mexico)

Becker-Ziaja, B.; Günther, S. et al. (2012). "Hospital-based surveillance for Lassa fever in Edo State, Nigeria, 2005-2008". Tropical Medicine & International Health17 (8): 1001–1004

Fehling Sarah Katharina, Frank Lennartz, and Thomas Strecker (2012). Multifunctional Nature of the Arenavirus RING Finger Protein Z. Journal of Virology, 4(11): 2973–3011.

Fisher-Hoch SP and McCormick JB (2011). Lassa fever vaccine. Expert review of vaccines.3 (2): 189–97.

Go, AS; Bauman, M; King, SM; Fonarow, GC; Lawrence, W; Williams, KA; Sanchez, E (2013). An Effective Approach to High Blood Pressure Control: A Science Advisory from the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention. Hypertension. 63 (4): 878–85.

Geisbert TW, Jones S, Fritz EA, et al. (2011). Development of a New Vaccine for the Prevention of Lassa Fever". PLOS ONE Medicine. 2 (6): e183.

Hastie, Kathryn M.; King, Liam B.; Zandonatti, Michelle A.; Saphire, Erica Ollmann; Menéndez-Arias, Luis (2012). Structural Basis for the dsRNA Specificity of the Lassa Virus NP Exonuclease. PLOS ONE, 7 (8): 1–8.

Idris Abdullahi Nasir and Fatima Muhammad Sani. Outbreaks, Pathogen Containment and Laboratory Investigations of Lassa fever in Nigeria. International Journal of Tropical Disease & Health 10(1): 1-10.

Marie-Laurence Moraz, Christelle Pythoud, Rolf Turk and Sylvia Rothenberger (2012).Cell entry of Lassa virus induces tyrosine phosphorylation of dystroglycan.Cell Microbiology, 15(5): 689–700.

Miquel Porta (2014). A Dictionary of Epidemiology (6th ed.). New York: Oxford University Press.

Oldstone Michael and Campbell Kevin (2011). Decoding Arenavirus Pathogenesis: Essential Roles for Alpha-Dystroglycan-Virus Interactions and the Immune Response. Journal of Virology,411(2): 170–179.

508 Okokhere Peter O., Cyril O. Erameh,and Francis Alikah (2018).Acute Lassa Virus Encephalitis
509 with Lassa Virus in the Cerebrospinal Fluid but Absent in the Blood: A Case Report with
510 a Positive Outcome.Journal of Virology, **86**:10811–10835.

511 Oppliger Joel, Giulia Torriani, Antonio Herrador, and Stefan Kunz (2016). Lassa Virus Cell
512 Entry via Dystroglycan Involves an Unusual Pathway of Macropinocytosis. Journal of
513 Virology, 90(14): 6412–6429.

514 Peterson, A. Townsend; Moses, Lina M.; Bausch, Daniel G. (2014). Mapping Transmission Risk
515 of Lassa Fever in West Africa: The Importance of Quality Control, Sampling Bias, and
516 Error Weighting. PLOS One. 9 (8): e100711.

517 Preston, Richard (2010). The demon in the freezer: a true story. New York: Random House.
518 ISBN 0-375-50856-2.

519 Price ME, Fisher-Hoch SP, Craven RB, McCormick JB (2011). A prospective study of maternal
520 and fetal outcome in acute Lassa fever infection during pregnancy. British Medical
521 Journal. 297 (6648): 584–7.

522 Public Health England (2016). Lassa fever: origins, reservoirs, transmission and guidelines
523 Archived 2 February 2016 at the Wayback Machine. First published: 5 September 2014.

524 Richmond, J. K. and Baglole, D. J. (2011). Lassa fever: Epidemiology, clinical features, and
525 social consequences. British Medical Journal. 327 (7426): 1271–1275.

526 Samuel, Daso (2017). Lassa fever... What you need to know.Journal of Virology, 86:10811–
527 10835.

528 Sogoba, N.; Feldmann, H.; Safronetz, D. (2012). Lassa Fever in West Africa: Evidence for an
529 Expanded Region of Endemicity. Zoonoses & Public Health. 59 (59): 43–47.

530 Tal Brosh-Nissimov (2018).Lassa fever: another threat from West Africa.Case Reports in
531 Neurological Medicine; 10(2): 150–158.

532 Werner and Dietrich (2004). Biological Resources and Migration. Springer. p. 363.
533
534 World Health Organization and Centers for Disease Control and Prevention (2014.). Infection

Control for Viral Haemorrhagic Fevers in the African Health Care Setting.

World Health Organization (2016). Lassa fever. World Health Organization, Geneva, Switzerland.

World Health Organization (2017). Target Product Profiles for Lassa virus Vaccine.Retrieved 11 September 2017.

World Health Organization (2018). Emergencies, Preparedness and Response: Lassa Fever Nigeria.

World Health Organization (2017) Target Product Profiles for Lassa virus Vaccine.

www.who/fact sheet/detail/Lassa fever (2017).

www.cdc.gov/vhf/lassa/index.htm (2018).

www.ncbi.nlm.nih.gov/books/NBK8142/(2018).

www.The Guardian (2017), Panic as LUTH confirms Lassa Fever outbreak in Lagos.

www.Thisday(2017) Lassa Fever: A deadly disease.

www.Sahara Reporters (2018). Nine dead as Lassa Fever Hits Ondo State.

www.premiumtimesng.com(2018). No Lassa Fever outbreak in Osun, State urges calm.

www.wikipedia.org/wiki/Lassa_virus, 2018.

Yun, N. E. and Walker, D. H. (2012). "Pathogenesis of Lassa Fever". Viruses. 4 (12): 2031–2048