Pathological Events of Lassa Fever Infection

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ABSTRACT

This chapter discusses the morphology, epidemiology, pathology, mortality risk factors, clinical manifestations, diagnosis, treatment, and prevention of Lassa virus (LASV) with a main focus on pathological events associated with the infection caused by LASV. Lassa fever (LF) also known as the viral hemorrhagic illness is caused by the LASV. It belongs to the family Arenaviridea. It is an animal-borne ailment spread by the common African rat. It is endemic in West Africa. It is a medium-sized virion that measures between 70 and 150 nm and is spherical. It is composed of two ambisense RNA segments. The natural reservoir of this virus is the Mastomys natalensis which is a common rat found in rural West Africa. Humans generally get an infection when they come into contact with the urine, feces, and respiratory secretions of the rats as the virus is shed in the secretions of the rats and also found in the blood. The prevalence of the antibodies to the lassa virus is 21% in Nigeria, 8 to 52% in Sierra Leone, and 4 to 55% in Guinea. LASV primarily affects the endothelial cells and utilizes the alpha-dystroglycan receptors. LASV suppresses the cells of the immune system and prevents the secretion of proinflammatory cytokines. Almost 80% of the patients do not show any kind of symptoms so LF is difficult to diagnose. Infected individuals may show acute to severe LF followed by multiple organ failure that can be seen in the spleen, kidney, and liver. The similarity of symptoms with other diseases is quite challenging in the recognition of the infected ones. Supportive treatment is the basis for the management of LF. Ribavirin is a broad-spectrum antiviral drug that is a guanosine analogue and owes a fine activity against LASV. In conclusion, LF is a crucial rodent-borne (zoonotic) illness. Suitable training of medical personnel and health care workers is essential in the treatment and prevention of infection. Vaccine development, preventive measures, and the development of drugs other than ribavirin or the modification of the existing drugs are the major suggestions to diminish LF.

Keywords: Viral hemorrhagic illness, Lassa virus (LASV), Ambisense RNA, Mastomys natalensis, Rodent-borne

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1. INTRODUCTION

The viral hemorrhagic illness known as Lassa fever (LF), caused by the Lassa virus (LASV). It is an arenavirus endemic in West Africa. Generally, it is spread by the common African rat and it is an animal-borne ailment. Lassa fever's first documented case occurred in Borno state of Nigeria in 1969 where two missionary nurses died because of LF and is named after the Nigerian town (Lassa), the virus is then isolated by Buckley and Cabals in 1970 (CDC 2022). It is noteworthy that nosocomial infections can affect healthcare workers as well (Chevalier et al. 2014). Throughout West Africa, it is endemic with a higher incidence in Sierra Leone, Liberia, Guinea, and Nigeria since *Mastomys natalensis*, the animal reservoir and vector of the virus is widely spread (Asogun et al. 2019). The endemic areas suffer considerably from the economic burden of this disease and public health officials around the world are concerned about potential importation (Garnett and Strong 2019; Kofman et al. 2019).

As the disease starts, it usually causes fever, general weakness, and malaise. Incubation period of LF ranges from 6 to 21 days. Flu-like symptoms may follow in a few days, including headache, chest pain, sore throat, cough, nausea, vomiting, diarrhea, and abdominal pain. Aside from facial swelling, there may also be pleural amd pericardial effusions, low blood pressure, and bleeding from the nose, mouth, vagina, or intestines in severe cases (Buckley and Cabals 1970; Asogun et al. 2019). Mortality and morbidity rates are considerably high in pregnant women suffering from lassa fever infection (Akpede et al. 2019; Kayem et al. 2020). Exposure to the excreta of the rodents and even butchering/hunting of the infected rodents can transmit disease to humans (McCormick et al. 1987; Ter Meulen et al. 1996; Newman 2021). Study findings from recent years (Lo Iacono et al. 2015) suggested that outbreaks are primarily driven by independent zoonotic transmission, whereas approximately 20% of cases result from secondary transmission, usually through spreading events in hospitals. Splenic, hepatocellular and adrenal necrosis and other histopathological changes in kidneys, lungs, and heart were observed on pathological examinations (Winn and Walker 1975; Walker et al. 1982; Hensley et al. 2011; Stein et al. 2021).

Even though Lassa fever gets its diagnosis from clinical criteria, laboratory confirmation is essential to confirm the diagnosis. Lassa fever is commonly diagnosed by enzyme-linked immunosorbent assays (ELISAs), which detect IgM and IgG antibodies and also LASV antigens. The best method for the early diagnosis of the disease is the reverse transcription polymerase chain reaction (RT-PCR) (Wiley et al. 2019) For treatment purposes, ribavirin is used. It is an antiviral drug with a broad spectrum of activity against LASV (Bausch et al. 2010). Oral and intravenous routes of transmission are used but the most preferred method is intravenous treatment as it shows a stronger effect in higher-risk cases. Control of rodents, avoiding direct contact, and consumption of rats are the main preventive measures against LASV (Ogbu et al. 2007).

This chapter aims to discuss the structure of the LASV, its epidemiology and prevalence in different regions, replication strategy, pathological events, complications caused by the virus, diagnostic approaches, zoonotic importance and mechanism of its transmission, current and developing methods of treatment of the infection, and the strategies to prevent and control the virus.

2. VIRUS MORPHOLOGY

This medium-sized virion measures between 70 and 150 nm and is spherical. A single-stranded RNA virus known as the LASV belongs to the Arenaviridae family (AV). All members of the family are composed of

two segments of ambisense RNA (genome that is used in both negative and positive sense capacities) and a nucleoprotein. This nucleoprotein is surrounded by a lipid envelope, which in turn contains a glycoprotein (Fig. 1). A sand-like particle inside the virus is traceable to ribosomes from the host, that is why it gets its name (Arena = sandy) via electron microscopy. The AV is classified based on their geographical distribution. They include the worldwide leukocytic choriomeningitis virus (LCMV), as well as the African LASV and Lujo viruses, all of which are not known to cause human disease. In particular, a new world virus is a group of viruses that are distributed across specific areas of the American continents, including the Junin, Guanarito, Machupo, and Sabia viruses, as well as other non-pathogenic strains (Yun and Walker 2012). As it contains two segments of single-stranded RNA the smaller RNA encodes the immature glycoprotein precursor and the nucleoprotein while the larger RNA segment encodes the Z protein and RNA polymerase which is RNA-dependant (Salvato et al. 1989; Eichler et al. 2003; Andersen et al. 2015).

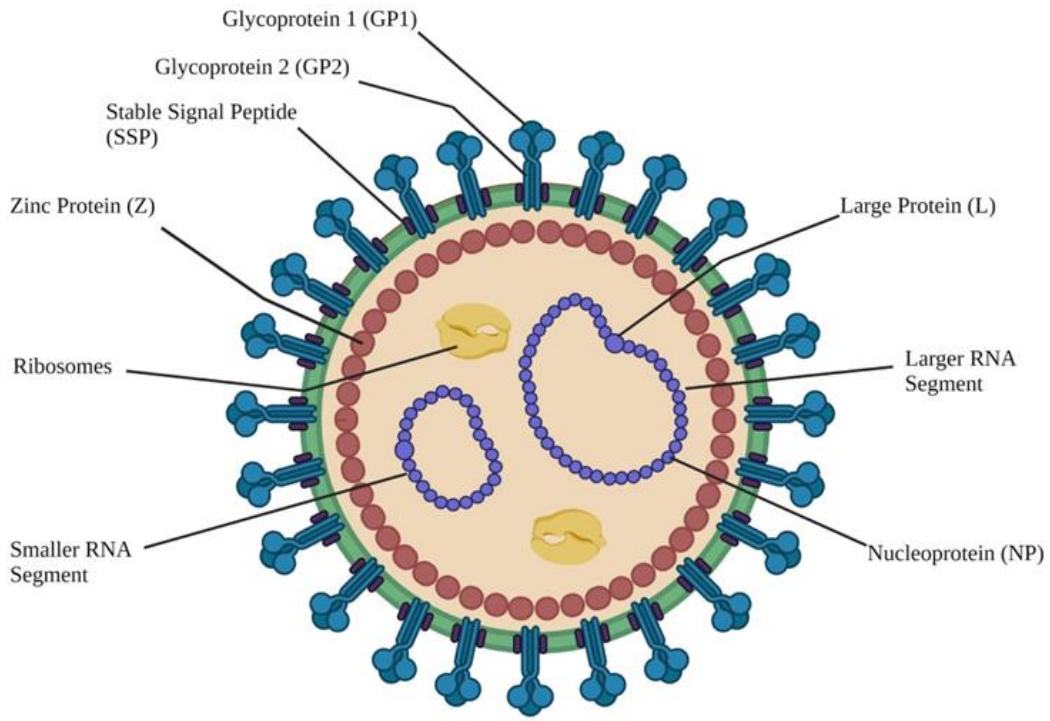

Fig. 1: Structure of Lassa Virus (Retrieved from BioRender)

3. EPIDEMIOLOGY

The virus is sustained in the environment by the rats that are chronically infected. The natural reservoir of this virus is the *Mastomys natalensis* which is a common rat found in rural West Africa. Humans generally get an infection when they come into contact with the urine, feces, and respiratory secretions of the rats as the virus is shed in the secretions of the rats and also found in the blood. Inhaling the dust contaminated with the virus or eating rats is also a source of infection (CDC 2015; Seregin et al. 2015). The virus may be shed in urine for 21-42 days and in semen for 3 months with a considerable risk of sexual transmission inspiring the survivors to use condoms (Richmond et al. 2003; CDC 2015; Seregin et al. 2015; WHO 2015). The regions in which the disease is endemic are Nigeria, Sierra Leone, and Liberia with seroprevalence rates of about 7% or more than 20% (Ogbu et al. 2007; Yun and Walker 2012). Confirmed cases were reported in Guinea, Mali, Senegal, Congo, Cote d'Ivoire, and Central African Republic (Fig. 2) (Richmond and Baglole 2003). Annually there is an incidence of about 100,000 to 300,000 cases out of these almost 5000 cases are fatal. In 2014 and 2015 two cases were reported in the United States (CDC 2015).

Fig. 2: Lassa fever: Outbreaks and Serological evidence of human infection (BMJ 2003) (Retrieved from BioRender).

The prevalence of the antibodies to the lassa virus is 21% in Nigeria, 8 to 52% in Sierra Leone, and 4 to 55% in Guinea (McCormick et al. 1987; Tomori et al. 1988; Lukashevich et al. 1993). The case fatality rate of lassa fever in the general population in Sierra Leone is about 70% and it is 20% in other developing countries (Keïta et al. 2019; Koch et al. 2021). Nigeria is also an endemic country. There is an increase in the number of cases that are confirmed because of poor sanitation, the presence of rodents that carry disease, and a lack of education and awareness among healthcare workers and the public (Fig. 3) (WHO 2023). So, the countries in which *Mastomys natalensis* is not commonly present generally have a less prevalence of the lassa virus. To stop the transmission of the virus in the prevailing countries people should avoid contact with the *Mastomys* rodents, keep the food in the containers that are rodent-proof, and by cleaning the houses to discourage the entry of rodents (Africa CDC 2019).

4. PATHOGENESIS OF LASSA FEVER

Lassa virus primarily affects the endothelial cells and utilizes the alpha-dystroglycan receptors to establish itself in the cells like macrophages, endothelial cells, and dendritic cells and these are the sites where the virus replicates. Lassa virus inhibits the manufacturing of interferons by the cells with the help of nucleoproteins (Fig. 4). Moreover, the LASV suppresses the cells of the immune system and prevents the secretion of the proinflammatory cytokines which include IL-8β, IL-6, and tumor necrosis factor (TNF-α) (Brosh-Nissimov 2016).

Receptors (alpha-dystroglycan) on the cell surface helps the virus to enter into the host cell. Alpha-dystroglycan is a very versatile receptor. LASV adopts a specific replication strategy called as “Ambisense” and it is very rapid. The early transcription of mRNA makes enough deposition of viral proteins that are required for the upcoming stage of replication. NP and L proteins are translated by the mRNA. Positive sense gene makes the copies of viral complementary RNA (vcRNA). Templates of RNA make the Negative-sense progeny. The mRNAs that are produced from the vcRNA are utilized to synthesize glycoproteins (GPs) and zinc (Z) proteins. At last temporal controls intensify the formation of spikes (Morin et al. 2010).

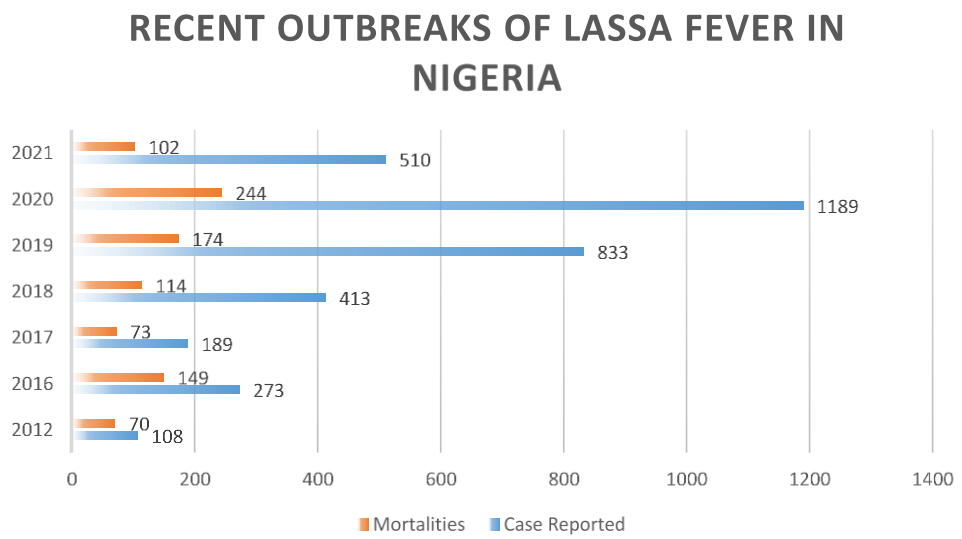

Fig. 3: Recent Outbreaks in Nigeria (Africa CDC 2019)

Initiation of the lassa fever infection occurs when an individual comes in contact with the excreta like respiratory secretions, urine, and saliva of the rat that carries the LASV. Antigen-presenting cells work as the focal points for the virus as it gets entry into the host cell. Most tissues of humans are infected by the virus causing multi-systemic complications, and stoppage of translocation of interferon regulatory factor-3 (IRF-3) (Rojek and Kunz 2008; Hastie et al. 2012). LASV halts the responses of interferon (IFN) as it has exonuclease activity. LASV utilizes pathogen-associated molecular patterns (PAMP) to find a way around the host's immune response (Azeez-Akande 2016). LASV mostly affects the blood vessels and cells of the reticuloendothelial system that are the sites of its replication and injures the capillaries. Bleeding in the lungs, brain, intestine, and myocardium can be observed (Günther et al. 2001; Ogbu et al. 2007).

Free expression of cytokines induced by the LASV is considered as the feasible mechanism of lassa fever pathogenesis. There is reported evidence of the fatal lassa fever in Germany in 2000 (Schmitz et al. 2002). The patient died because of multiple organ failure and development of shock which is because of hemorrhage and clinical findings showed that there is a high level of the interferon-γ (IFN-γ), tumor necrosis factor-α (TNF-α), and proinflammatory cytokines. Although, no elevation in cytokines can be seen in another case study of lethal LF. This indicates that the concentrations of TNF-α and IFN-γ increased for a brief duration or in a few patients (Mahanty et al. 2001; Yun and Walker 2012). Therefore, LF does not exhibit a "cytokine storm" as it is apparent in other hemorrhagic fevers (Ogbu et al. 2007; McLay et al. 2014).

Additionally, the organized suppression of the immune system by the virus is somehow related to the pathogenesis of the LF (Lukashevich et al. 1999). When there is an infection of LASV, the dendritic cells (DC) and macrophages (MP) fail to activate. Infected DC shows malfunctioning and is unable to produce the proinflammatory cytokines (Mahanty et al. 2003; Baize et al. 2004). Mopeia virus which is a non-pathogenic arenavirus, also affects the DC and has a 75% amino acid sequence resemblance with the LASV and has the same rat reservoir (Bowen et al. 1997). Mopeia virus can cause stronger responses of T-cells (Pannetier et al. 2011).

The principal pathological change is in the capillary permeability, along with the development of hypovolemic shock and edema, necrosis of the liver, adrenals and spleen, and hepatitis is also observable (Ogbu et al. 2007; McLay et al. 2014). Immune response against the LASV is not thoroughly acknowledged. Cell-based immunity is very essential with efficient responses of T-cells in the survivors (Yun and Walker 2012). Responses of antibodies are less essential, however, there is an early production of the antibodies, and neutralizing antibodies emerge after weeks or months and have low avidity and titers (Seregin et al. 2015).

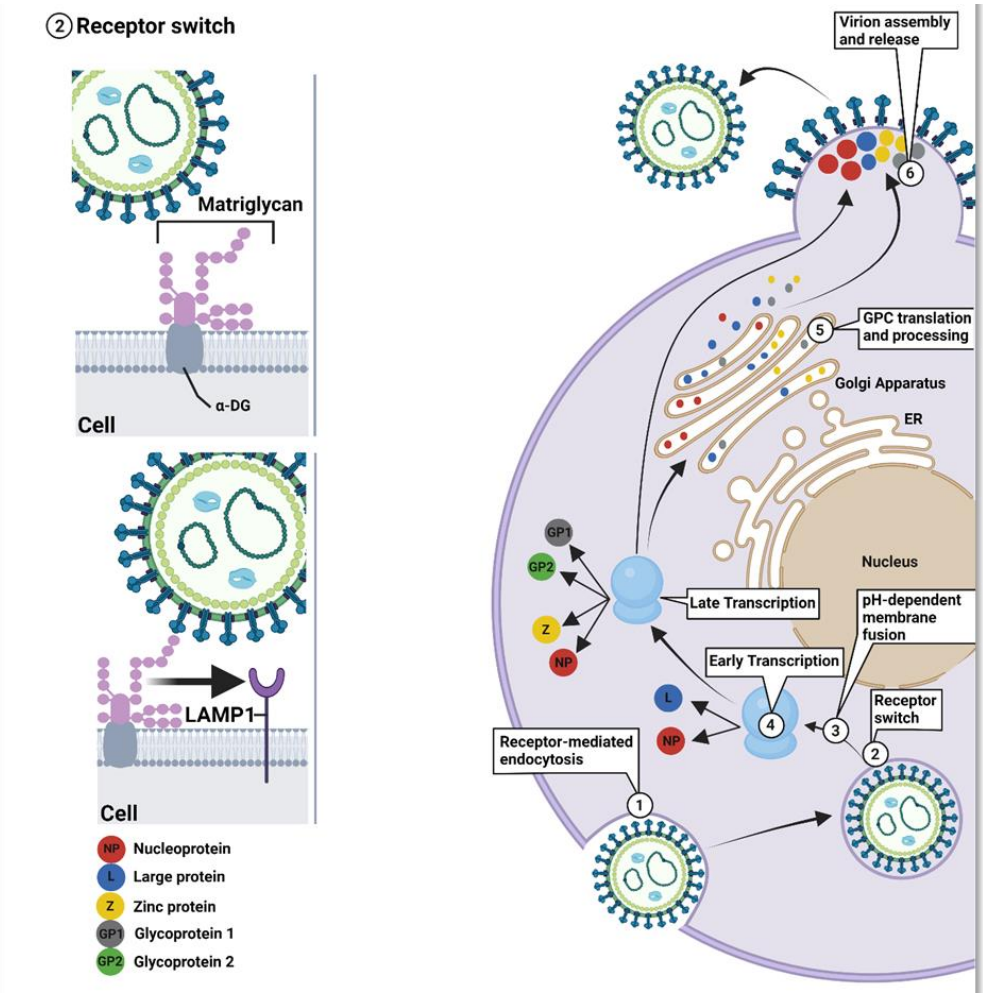

Fig. 4: Replication strategy of Lassa virus (Retreived from BioRender)

5. ZOONOTIC PERSPECTIVE AND TRANSMISSION OF LASSA VIRUS

Lassa fever (LF) is a zoonotic disease (McCormick and Fischer-Hoch 2002; Günther and Lenz 2004; Fichet-Calvet and Rogers 2009). The primary reservoir of LASV is *Mastomys natalensis* which is a multimammate mouse. Some other reservoirs (*Hylomyscus pamfi* and *Mastomys erythroleucus*) have also been currently recognized (Olayemi et al. 2016). The participation of these two species in human infections is still unknown. LASV can spread between *Mastomys natalensis* via vertical or horizontal routes (Fichet-Calvet et al. 2008; Fichet-Calvet et al. 2014).

Transmission through rodents into humans generally occurs due to direct contact with the fluids like blood, saliva, and urine and indirectly via foodstuffs and surfaces polluted with these fluids (McCormick 1999; Ogbu et al. 2007). Urine may exhibit a certain threat of infections in humans as the *Mastomys natalensis* can cast LASV in the urine at any time of their age (Walker et al. 1975; Borremans et al. 2015). LASV can be converted into a fine mist in the laboratory (Stephenson et al. 1984). In living areas and hospitals, contact with the fluids of the human body is a common source of infection transmission and approximately occurs in 20% of the cases (Fig. 5). Chances of disease development because of zoonotic transmission are generally connected with the consumption and hunting of rodents (Ter Meulen et al. 1996; Bonner et al. 2007; Bonwitt et al. 2016). While shaking hands, hugging, and sitting together are not a source of LASV transmission (WHO 2015).

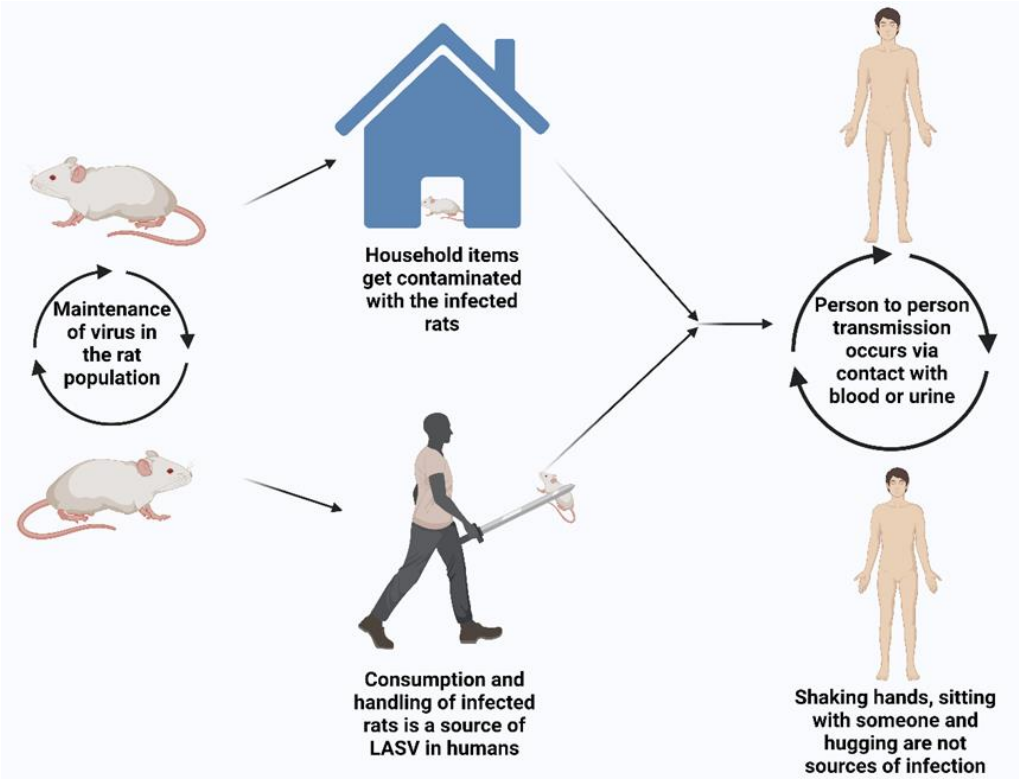

Fig. 5: Transmission of Lassa virus (Retrieved from BioRender)

6. MORTALITY RISK FACTORS

The rate of case fatality in patients is almost 30%, who are presented to the health care environments (Kenmoe et al. 2020; Merson et al. 2021). Chances of death are greater in pregnant women and even higher in the third trimester (Price et al. 1988; Kenmoe et al. 2020). About 90% of total pregnancies can be lost in pregnant women infected with LF (Wauquier et al. 2020). Children infected with LF and who have positive antigen tests confront high mortality (63%) (Samuels et al. 2021). The mortality rate in severe cases of LF is generally between 1 to 15% (WHO 2023). The possible risk factors for high mortality rate are enlisted in Fig. 6.

7. CLINICAL MANIFESTATIONS OF LASSA FEVER

The way of clinical indications is not specific and this creates difficulties for clinical examination. The rats that are zoonotic hosts carry the virus and do not show any symptoms of disease but they shed the virus in their feces, urine, and other secretions. Almost 80% of the patients do not show any kind of symptoms (Richmond and Baglole 2003; Johnson et al. 2019). Infected individuals may show acute to severe LF followed by multiple organ failure that can be seen in the spleen, kidney, and liver (McCormick et al. 1987; WHO 2021). Duration of clinical symptoms is 1 to 4 weeks. The indications of LF are similar to other diseases like typhoid and malaria which may be confusing. The similarity of symptoms with other diseases is quite challenging in the recognition of the infected ones (Akhuemokhan et al. 2017; Okokhere et al. 2018). Evolution of LF symptoms is given below (Table 1).

Death of the infected individual may occur in 14 days if there is multiple organ failure (CDC 2019). Long-term after-effects like hearing loss is a major social and economic burden in West Africa. In Nigeria, $43 million are used annually for aid programs (Mateer et al. 2018).

Table 1: Evolution of LF symptoms (WHO 2018).

Infectivity	
Days	Symptoms
1-3	Fever Extreme fatigue General weakness Headache
3-6	Severe throat Diarrhea Vomiting Face swelling
6-9	Low blood pressure Nose bleeding

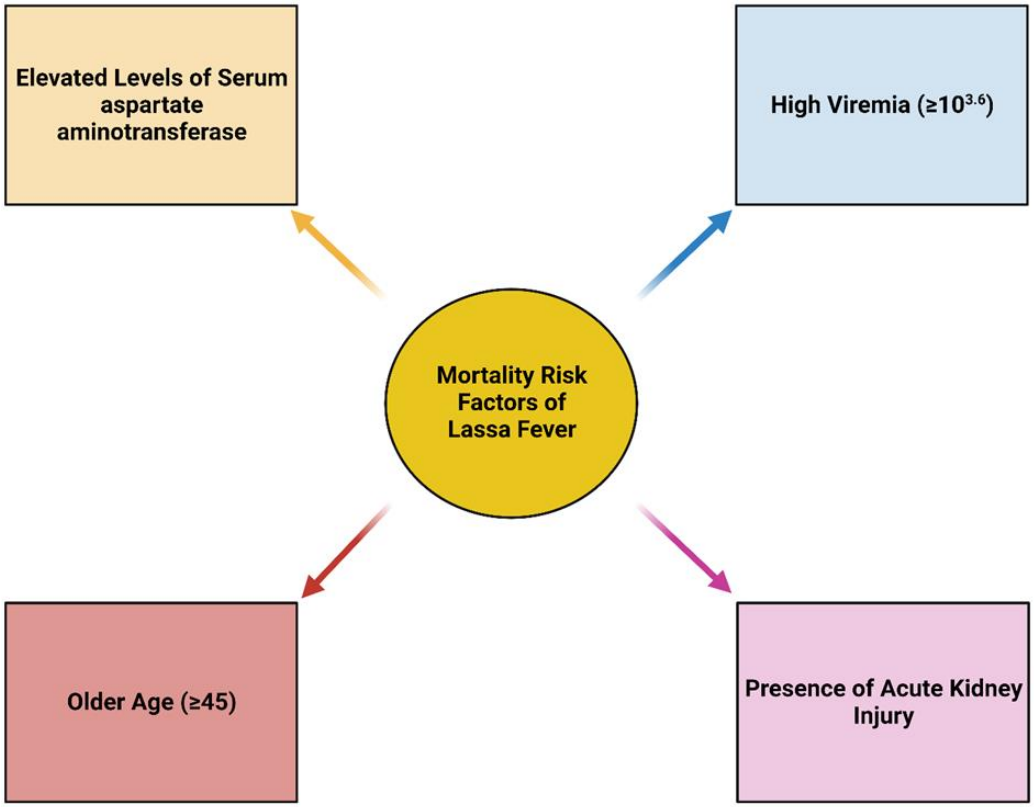

Fig. 6: Mortality Risk Factors of LF (McCormick et al. 1986; Okokhere et al. 2018; Adetunji et al. 2021) (Retrieved from BioRender).

There is an indication of exudative pharyngitis on the clinical inspection of the throat of the patients that are infected with the LASV and the inspection of the urine samples generally shows the presence of the proteins. There is also a decrease in the number of neutrophils. Meningitis, tremors, and convulsions are neurological signs that are not generally visible. Strong evidence from the 441 infected individuals showed that the prime indication of LF is pharyngitis, proteinuria, aggregation of fever, and retrosternal pain. Vomiting and sore throat are also observable (McCormick et al. 1987; CDC 2019). In addition to these conditions, effusion of pericardia, the 8th nerve deafness, and bleeding of mucosa were described as 2%, 4%, and 17%, respectively. Nausea, diarrhea, pleural effusion, and facial edema are also visible in the lassa fever. Factors like poor sanitation and bad social habits are considered as alarming components that can increase the dissemination of the ailment (Okokhere et al. 2009).

Individuals infected with LF generally show no visible symptoms and may remain unrecognized. People of this category and the survivors of acute LF infection may develop loss of hearing to various extents. Bilateral loss of hearing is most common and can affect all extents of hearing (Ibekwe et al. 2011). Around 25% of individuals are at risk of infection upon exposure to LASV (WHO 2000). The development and origin of this diminution in hearing are postulated to arise because of an immunological reaction among the plasma membrane and circulating LASV immunoglobins in the cell at its basal side (Okokhere et al. 2009). Yun and his colleagues in 2016 accustomed a model from muridae (the largest family of rodents and mammals) which exhibits several features of LF that are also visible in humans (Yun et al. 2016). The virus isolated from lethal cases was extremely virulent and the virus that is isolated from the non-lethal cases showed mild disease and low mortality but, in both cases, the surviving ones developed a condition called sensorineural hearing loss (any cause of hearing loss due to pathology of the cochlea, auditory nerve, or central nervous system). Recently, Maruyama and his colleagues conducted an evaluation of the auditory function engaging the distortion product otoacoustic emissions (DPOAE) (generated by cochlea when the ear is dispensed with the two concurrent pure tones) and auditory brainstem response (ABR) (that generally checks the brain's response to the sound) in determining the mechanism of the LASV-prompted hearing loss. They calculated the values of the above-mentioned tests in some rodents and deduced that the exhaustion of CD4 T-cells plays an important role in hearing loss prompted by LASV and CD8 T-cells take part in acute phase and pathogenicity of LASV (Maruyama et al. 2022).

8. DIAGNOSIS

Lassa fever is difficult to recognize especially in the early stages as 80% of the patients are asymptomatic, so laboratory diagnosis is essential in such cases for the initiation of the specific treatment. Commercial and laboratory-made assays are available but the testing of LASV is still restricted to the West African laboratories (Asogun et al. 2012; Akhuemokhan et al. 2017). The best way for the diagnosis of LASV is the polymerase chain reaction (PCR) out of the blood. 1st day of hospitalization reports 79% sensitivity, escalating to 100% on the third day (Richmond and Baglole 2003; Ogbu et al. 2007; Seregin et al. 2015). Variation in the genetic strains hardly guides to false negative outcomes (Panning et al. 2010). Different serological tests are being utilized which include direct nucleoprotein antigen testing and IgM and IgG antibodies against nucleoproteins (NP) and glycoproteins (GP). A mixed IgM and NP enzyme-linked immunosorbent assay (ELISA) has a specificity of 90% and a sensitivity of 88% (Richmond and Baglole 2003). The persistence of IgM is for months or even years, and IgG can persist for decades (Bond et al. 2013). There is the existence of cross-reactivity with the lymphocytic choriomeningitis virus (LCMV) which is also a member of the Arenaviridae family and its primary host is, *Mus musculus,* the common house mouse (Haas et al. 2003). A qualitative quick indicative test (rapid diagnostic test) (RDT) that requires no instrumentation is also available and is perceptibly elucidated by the user (Boisen et al. 2018; Boisen et al. 2020). Clinical samples from the patients of LF are hazardous to the laboratory personnel because contact with the mucosal surfaces and the percutaneous inoculations are the main risk factors of the infection. So higher level of safety for the processing and collection of samples is required. Isolation of LASV requires extreme biosafety conditions (CDC and NIH 2009).

9. TREATMENT

Supportive treatment is the basis for the management of LF. The main aim is the rejuvenation of the volume that accounts for third spacing (too much fluid movement from blood vessels towards the

interstitial space) as the overload of volume can cause pulmonary edema. Respiratory support and electrolyte balance are the other goals of treatment (McCormick et al. 1986; Ölschläger and Flatz 2013).
Ribavirin is a broad-spectrum antiviral drug that is a guanosine analogue and owes a fine activity against LASV. Plasma concentration is considerably higher in case of intravenous treatment with standard doses as compared to minimal inhibitory concentration (lowest concentration of drug that inhibits the visible growth of microorganisms) but the oral treatment is limited because of 50% bioavailability and has considerable side effects (Bausch et al. 2010). Controlled clinical trials were performed by CDC in the 1980s in Sierra Leone in which they assessed the gains of oral and intravenous ribavirin (McCormick et al. 1986). Both intravenous and oral ribavirin are beneficial. Recommended intravenous dose is 2.4 g followed by a 1g dose every 6 hours for almost 10 days (recommended in average-weight adults). Ribavirin is not effective if it is administered after physiological dysregulation or viremia peak (McCormick et al. 1986).
A major adverse effect of ribavirin is dose-dependent hemolysis (a blood disorder in which a medicine triggers the immune system to kill the red blood cells) appearing in almost 20% of the patients and decreasing the hematocrit level (proportion of red blood cells in the blood) (McCormick et al. 1986; Duvignaud et al. 2021). There are many other adverse effects associated with the oral treatment like diarrhea, vomiting, nausea, dry mouth, fatigue, myalgia, metal taste, headache, rashes, thrombocytosis, insomnia, mood changes, jaundice, and increased lipase level but no mortality was declared after treatment with the ribavirin (Bausch et al. 2010). Ribavirin is embryotoxic and teratogenic in rodents. It is generally contraindicated during lactation and pregnancy (Sinclair et al. 2017).
For the treatment of lassa fever some other small molecular drugs are under consideration (Hansen et al. 2021). A small molecular purine analogue Favipiravir (T-705) is considered more efficient than ribavirin in the treatment of LASV (Gowen et al. 2010; Mendenhall et al. 2011; Safronetz et al. 2015; Oestereich et al. 2016; Rosenke et al. 2018; Lingas et al. 2021). Currently, no approved vaccine for LASV is available but there are many vaccine platforms that show efficacy in animal models that have been developed and some have recently entered the first phase of human clinical trials (Salami et al. 2019).

10. PREVENTION AND CONTROL

The important preventive measure in endemic areas is the control of rodents in and around the residences and avoiding contact and consumption of the rats (Ogbu et al. 2007). Avoid contact with infected persons and health care workers if the maintenance of infection control practices is poor. Acquisition and transmission of LASV can also be controlled and prevented by implementing some measures that include the establishment of a task force, policy formulation, reducing the LF at the national and state level, and the formation of committees for monitoring. Additionally, there should be awareness among the general public and healthcare workers about the transmission, symptoms, disease dynamics, and preventive measures. This disease can be controlled by prohibiting the spread of zoonotic host and by shunning rat hunting and consumption, obstruction of the hiding places of rodents, and use of the snares in the homes to diminish their number. Other preventive measures comprise healthy and good personal hygiene, proper disposal of waste, good environmental sanitation, and shunning of food scattering by the roadside or in areas where rats can gain access to this food and also storing the food items in rat-proof containers (Ogoina 2013). General strategy to control LF outbreaks is given in Table 2.
Control of hospital infection is the main focus when dealing the imported cases in the Western world as there are many nosocomial outbreaks of LF in Africa. Inhibiting the use of contaminated needles and avoiding the direct contact with the blood and secretions of patients can also prevent the transmission of the virus. Lack of personal protective equipment, reuse of needles, and surgery performance in poor hygienic conditions are major sources of disease in endemic areas (Fisher-Hoch et al. 1995; Yun and Walker 2012). Hospitals in Africa where preventive measures are followed, have less seroprevalence for LASV as compared to the neighboring rural community (Helmick et al. 1986).

Table 2: General strategy to control lassa fever outbreaks (WHO 2018).

Coordination			
Psycho-social support		Control of reservoirs and vectors in nature	
Social and behavioral interventions	Clinical case management	Logistics	Epidemiological investigation and surveillance
Conduct cultural and social assessments	Triage in/out	Security, police	Active case-finding
Formal and informal connections	Barrier nursing	Lodging, food	Follow-up of contacts
Address community concerns	Infection control	Epidemiological and	Specimens
Engage with influencers: traditional	Organize funerals	social mobile teams	Laboratory testing
healers, local authorities & religious	Clinical trials	Finances, salaries	Database analysis
leaders	Ethics committee	Transport vehicles	Search for source

11. CONCLUSIONS

LF is a crucial rodent-borne (zoonotic) illness that has validated the epidemiological progression and proportion in the sub-region of West Africa. International travels considerably increase the possibilities of transmission of LASV to several other zones of Africa. An unstable economy and limited resources are the major factors that hinder the management of current and emerging contagious diseases in the region. Suitable training of medical personnel and health care workers is essential in the treatment and prevention of infection. The transmission of LASV is very simple and can easily be prevented. Majority of the infected individuals are asymptomatic and the general symptoms of the disease are correlated with several other ailments, so the diagnosis is difficult in the initial stages. In endemic areas, ribavirin is provided in health care centers and hospitals particularly at the onset of the disease because it is very effective in the progressive stages of the disease. Vaccine development, preventive measures, and the development of drugs other than ribavirin or the modification of the existing drugs are the major suggestions to diminish LF.

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