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Re-Emerging Lassa Fever Outbreaks: Epidemiological Analysis, Preparedness, and Prevention

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Review

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Abstract: Lassa fever, commonly known as Lassa hemorrhagic fever (LHF), is one of the progressive illnesses invading a large population of two to three million individuals in West Africa. The infection transmitted through the rodents severely impacts the local population and the medical professionals in surrounding areas, which were also the primary target of LHF. In epidemic areas, Lassa fever causes a public health threat since it poses a significant morbidity and fatality Case rate (CFR) ≥ 50%). The disease is widespread in West Africa and has developed into one of the most common and life-threatening viral hemorrhagic fevers. Monitoring and preventing persistent disease outbreaks has been challenging in affected regions due to insufficient healthcare facilities, diagnostics labs, care centers, and low socioeconomic conditions. An absence of public awareness and the emergence of an ecological niche is advantageous for the survival and multiplication of the mouse (*Mastomys natalensis*) inhabiting the Lassa virus serving as the disease's natural host and reservoir. The current review focuses on early diagnosis and appropriate treatment, highlighting the immediate requirement of clinically approved vaccines for LHF, causing preventative and control actions more difficult in the present era.

Keywords: Lassa fever; epidemic; epidemiological analysis; pathogenesis; prevention

1. Introduction

The single-stranded, encapsulated, bipartite virus, popularly identified as the Lassa virus, is a member of the *Arenaviridae* family of virus class [1]. This RNA virus is a spherical or rounded pattern with a standard diameter of 110 to 130 nm. In cross-section, they appear to be "sandy or grainy particles" (host cell-derived ribosomes). The RNA genomes encode four proteins: the smaller segment's precursor nucleoprotein and glycoprotein, and in the more significant segment RNA-dependent RNA-polymerase and matrix RING Zinc-finger protein [1,2]. The incredibly complex nucleotide diversity that the Lassa virus requires among strains is closely linked with the aggregation of strains among different geographic locations. As a result of investigations, six major clades or lineages of ***Lassa mammarenavirus*** (**LASV**) have been identified, including Clades I to III in Nigeria, Clade IV in Sierra Leone, Guinea, and Liberia, Clade V in southern Mali, and Clade VI, which is a most upcoming lineage that is emerging from Togo [3]. These strains have such a distinctive quality considered as the capability to alter over time. There are now seven lineages after the current Nigerian Lassa fever epidemic resulted in discovery of an entirely new lineage [4,5]. The significant genetic variability of the Lassa virus affects the development of diagnostic molecular tests and a universal vaccine for Lassa fever. This variability makes it challenging to create a diagnostic test or vaccine that can be effective in different geographic locations, regardless of the specific strain of the virus that is present [5–7]. It could also influence how an infection appears clinically and how severe it is [8–13].

Mastomys natalensis, a "multimammate rat," is presumed to be the LASV animal reservoir. It is a rodent belonging to the genus *Mastomys*, which is widely spread and most often reproduces in West Africa [14–16]. The rats get the infection while still in the fetus and retain it throughout their lives. Rats with LASV infections do not get sick but excrete the virus in their urine and feces. *Mastomys erythroleucus* and *Hylomyscus pamfi*, two recently found rodent reservoirs, might impact how LASV and Lassa fever cases are spread over time even though *M. natalensis* was previously thought to be the natural reservoir of the virus [16,17].

2. Mode of transmission of Lassa virus

Direct or indirect contact with rodents (LHF) (Lassa fever) induces the primary or initial infection in humans [16,18,19]. People living in rural environments, where *Mastomys* rats are typically found, are at a higher risk of contracting (LHF) or Lassa Infection, particularly in neighborhoods with subpar hygienic standards or crowded housing [13,20–22]. During the dry weather, *Mastomys* rats break into people's houses in need of food. Infection with LASV in humans is carried out by exposure to the urine, feces, blood, or fleshes of Mastomys rats infected with the disease. Direct

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contact with these harmful substances, which can occur when persons come in contact with offensive materials, contaminated food consumption, or interact directly with open wounds or sores, can lead to infection [22–26]. People residing in overcrowded homes, families looking for a sick member, and local communities participating in funeral customs have all been linked to the spread of secondary infection (person-to-person) among humans.

3. Pathogenesis and virulence factors

LASV is an enveloped negative-sense, single-stranded RNA virus. The genome has two ambisense regions (the large and small segments). RNA polymerase (L) and a zinc-binding protein (Z), which is comparable to the matrix protein in other RNA viruses, are both encoded by the significant segment [27]. The brief portion encodes the envelope glycoprotein and nucleoprotein (NP) (GPC) combination. An intergenic (IGR) non-coding region that forms a stable loop divides each segment's coding sections from one another (hairpin) [28]. The IGR participates in viral assembly or budding and structure-dependent transcription termination.

The primary structural protein, known as the NP, is made up of nucleocapsid proteins crucial for viral RNA replication, transcription, and virion formation. By attaching to the kinase domain of IKK-e, it is employed to avoid the innate immune response's RIG-I-like pathway [29]. The LASV genome's NP region, which has undergone the greatest sequencing, aids in differentiating different strains and lineages. The envelope protein, which facilitates viral attachment and cell penetration, is produced by the GPC. The mature virion's lipid bilayer is proteolytically transformed into a heterotrimer by the host cell subtilizing SKI-1/S1P. Each heterotrimer contains a myristoylated stable signal peptide (SSP) necessary for GPC processing and function, a GP2 class-I membrane fusion protein, and a receptor-binding GP1 domain [30]. While the Z protein helps to create the virions' matrix layer, the L RNA polymerase is responsible for transcription and replication. The pathogenesis mechanism is summarised in Figure 1.

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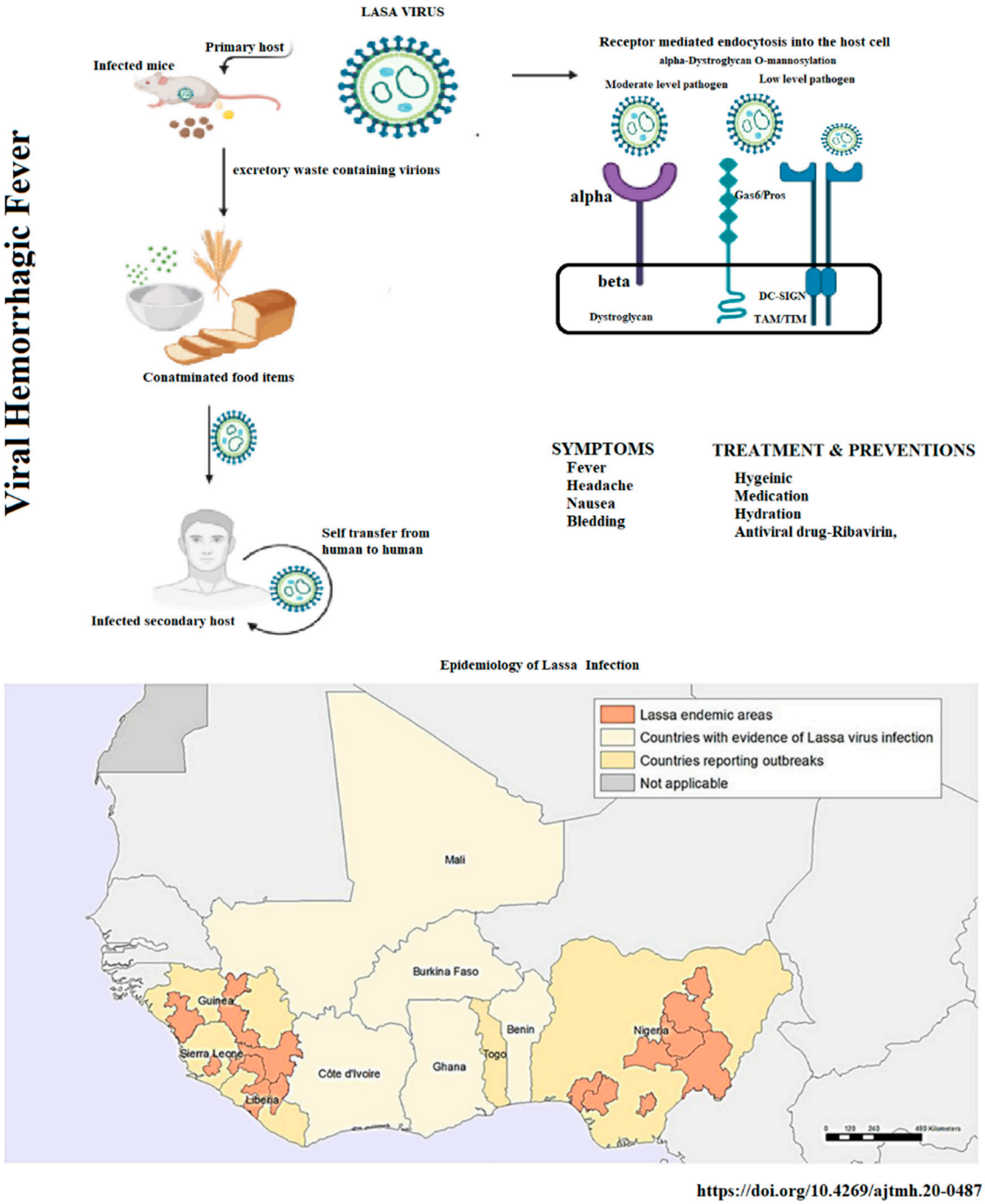

Figure 1. Schematic presentation of Lassa fever pathogenesis, symptomology, treatment, and epidemiological aspect at a global platform.

4. Clinical Features

However, human-to-human transmissions can also raise it; a large number of (LHF) cases are introduced by rodent-to-human LASV transmissions caused by direct exposure to infected animals or animal wastes [31]. Even though LASV infection can induce ailments in humans, it is believed to cause asymptomatic infection in its natural animal reservoirs, including the multimammate rodent species *Mastomys natalensis*, *Mastomys erythroleucus*, and *Hylomyscus pamfi*, as well as in rodents that have been experimentally infected with the virus, including *Mus musculus* (house mouse), *Rattus rattus.* This shows that LASV and the wild rodent species potentially acting as the virus' reservoirs have long coevolved [32]. In West Africa, the peak of (LHF) is high in dry seasons, and then in the wet seasons, it lowers in comparison.

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The incubation period for (LHF) lasts 7 to 21 days (1-3 weeks) after exposure to infection. According to the WHO, 80% of LASV-infected persons remain asymptomatic, while only 20% of affected patients develop severe, multisystem diseases [33]. Clinical diagnosis of (LHF) can often be challenging because the initial signs and symptoms of (LHF) are generally mild and appear to be the same as those of other enteric fevers. Persons native to West Africa or individuals who have recently traveled to a region where (LHF) is recognized to be widespread and suffer from a fever above 38 °C (100.4 °F) should be considered for suffering the illness if their condition does not continue improving after getting antimalarial or antibiotic treatments [34]. Mild (LHF) patients typically suffer flu-like signs, such as fever, achiness, fatigue, and headaches.

Joint discomfort, lower back pain, a dry cough, and a sore throat frequently follow as the disease worsens in its early stages. 70% of people with severe (LHF) have pharyngitis, which can cause patches of yellow to white discharge to develop on the tonsils in the form of a pseudo membrane [34]. Patients with symptomatic (LHF) have diarrhea, vomiting, and stomach pain in 50% to 70% of cases. After the commencement of symptoms, minor illnesses often recover 8–10 days later. However, 6–10 days following the virus infection, severe (LHF) patients quickly worsen. It is possible to anticipate the course of a disease from specific types of symptoms and viremia levels. A life-threatening outcome is 21 times more likely in patients with serum viral titers, more significant than $\mathbf{10^3}$ tissue culture infectious dose TCID50/mL. TCID50 is the virus concentration that infects 50% of the target cells in mammalian cell culture) and high levels of aspartate aminotransferase (AST, a cellular enzyme indicative of tissue damage). The number of viremia peaks 4–9 days after the beginning of symptoms but declines as the virus leaves the blood, typically three weeks after symptoms first appear. But persons with severe (LHF) symptoms and high viremia levels frequently fail to trigger an adequate immune response to restrain viral spread, which eventually has a lousy prognosis or even leads to death.

Severe (LHF) instances are frequently accompanied by increased vascular permeability, leading to face edema, pleural effusions, and pericardial effusions. Acute respiratory distress with laryngeal edema and fluid buildup in the lung cavity can also occur in severe (LHF) patients. Mucosal hemorrhage occurs in 15%–20% of extreme (LHF) instances with low blood pressure. Death frequently follows hypovolemic shock and encephalopathy symptoms within 14 days. In the later phases of the illness, disorientation, abnormal walking patterns, convulsions, comas, and seizures are also conceivable; some patients even have tremors just before passing.

5. Phases or outbreaks of Lassa Fever Outbreaks in Nigeria

A viral hemorrhagic fever spread across several regions of West Africa, primarily Liberia, Nigeria, Guinea, and Sierra Leone, the Lassa virus (LASV), is a zoonotic, acute, deadly disease-causing virus [35]. The leading viral pool of LASV is *Mastomys natalensis*, a multimammate rodent found in ample numbers across various regions of West Africa. Although the first individual case of Lassa fever was reported in 1969, previous research studies indicate that this kind of viral agent's endemic transmission to humans has been carried on for more than a century. Even today, it is a significant public health concern in parts of West Africa, with 3 million cases of infection and around 67000 annual deaths. The genetic diversity of this virus proves to be the greatest challenge to the researchers and the medical world that have been working on its diagnosis and treatment.

The viral disease is now called "Lassa fever" since the first symptom of the ailment was diagnosed in the remote town of Yedseram River valley of Lassa in northeastern Nigeria [36]. The first affected individuals were missionary nurses by profession who were infected during their work in a rural clinic in this region; they died eventually. Soon a third nurse fell ill and was evacuated to a hospital in New York City but survived the infection. The antibody-rich plasma from her body was used later. Blood and other samples from these infected nurses were examined in Arbovirus Research Unit at Yale University, wherein the novel virus was successfully isolated. Two researchers at the research unit were infected; one died, and the other survived after receiving blood from passive immunotherapy from the nurse who had previously survived the infection.

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Since then, there have been several outbreaks of Lassa fever in different regions of Nigeria, including Jos, Onitsha, Zonkwua, Abo Mbaise, Owerri, Epkoma, and Lafiya. Following consideration in the 1970s and 1980s, Nigeria's three major Lassa fever transmission areas were the region around Lassa in the north-east part and Jos in the central [37]. The dry season is the optimum time for transmitting Lassa fever, which usually peaks between December and February [38]. In 1970-1972, three epidemic outbreaks occurred in distinct regions of Western Africa, including Nigeria, Liberia, and Sierra Leone. The previous two epidemics often involved nosocomial transmission, while the third was community-based [39].

Another incident of Lassa fever was observed in Nigeria in 1989. The inflicted man, a 43-year-old individual native from Nigeria but who lived in the US for 11 years at the time, was infected. His mother passed away in Nigeria from severe febrile sickness; shortly after that, a similar developed in other family members. The man reached his family in Nigeria in January 1989 when his mother was extremely ill. In February, he appeared with severe influenza-like symptoms similar to Lassa fever. Shortly after he died from other complications, a post-mortem identified and confirmed the Lassa fever antigen. Examinations at different levels were conducted to determine and monitor interactions, and affected persons were cared for.

A hospital-based investigation was carried out in Irrua in 2003 and 2004 to obtain better insights into the spreading of this pandemic viral illness in the Edo state of Nigeria [4]. The examination was established in the University of Lagos laboratory, where multiple samples were examined, and tests were evaluated at different levels [40]. Depending on the reported findings, about 6% of the febrile patients used to have a confirmed LASV infection. In 2005, the Abakaliki, Ebonyi State Hospital mentioned 4 cases, including a male and three women, among which only one lady recovered. At the Jos Plateau State Hospital, a 19-year-old girl appeared with the disease and eventually died in 2007. A person aged 37 and two men aged 38 died from this dangerous illness in 2008. Moreover, two males out of 30 developed the disease and were examined at the Jos, Plateau State Hospital, among one of them recovered.

Between January and April of 2016, there was a remarkable rise in the overall number of LASV infections in Nigeria, with 268 identified and reported cases and 147 mortalities. Disease was discovered to be transmitted among 23 of the 36 states in Nigeria [41]. In the same region in 2018, Lassa fever infectious cases rose significantly, which was subsequently determined to be multifactorial and not the cause of a new strain. The vast majority of the individuals affected in Nigeria are between the ages of 21 and 30 as of the 42nd week of 2022. The number of identified and reported cases gradually increased compared to the same period in 2021.

Table 1. The annual variation in the number of cases and deaths caused due to Lassa fever, 2001-2022.

Year	No. of patients (approx.)	No. of deaths (approx.)	n (%) of deaths	References
2001	6150	16	0.3	[70]
2002	8850	23	0.3	
2003	9092	22	0.2	
2004	8388	25	0.3	
2005	9215	65	0.7	
2006	11060	54	0.5	
2007	11644	56	0.5	
2008	13617	38	0.3	
2009	12292	56	0.5	
2010	12374	76	0.6	
2011	11537	62	0.5	
2012	13589	113	0.8	
2013	10969	83	0.8	
2014	8671	67	0.8	

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2015	10793	31	0.3	
2016	9566	102	1.1	
2017	11537	161	1.4	
2018	7363	248	3.4	
2019	8392	154	1.8	[71]
2020	7390	244	3.1	[72]
2021	4214	80	1.8	[73]
2022 (42nd week)	8268	177	2.1	[74]

Due to a lack of extensive evaluation of testing, there are only limited and incomplete data for years before 2000 about Nigerian Lassa fever. The occurrence of the widespread virus in Nigeria and the unavailability of comprehensive information on the infection's progression patterns have always been far apart. However, the reported data that are now available suggest that the outbreaks of this potentially fatal illness have been mitigated dimensionally and temporally and are assumed to exhibit themselves for the indigenous of Nigeria and other places of West Africa in an even more devastating manner.

6. Factors Contributing to re-emergence of Lassa Fever epidemics

6.1. Nosocomial transmission

The outbreak of Lassa fever was first identified in different healthcare centers where the virus spread through nosocomial transmission. This occurred due to inadequate infection prevention and control procedures [42]. The virus spread in hospitals and then into different communities due to unprotected contact with other bodily fluids, using a single needle in multiple patients, poor sanitization and sterilization of the medical equipment, etc. The inadequate measures for preventing LASV infection and control measures within the countries partially result in the need for more support and funds for the public health system.

6.2. Travel and Migration

Disputes in Liberia, Nigeria, and Sierra Leone urged people to migrate from unsafe locations to refugee communities. By this, the migrants were forced to live in dirty and congested refugee settlements or camps. The surroundings and atmosphere were most appropriate for the proliferation of LASV due to these living circumstances. Large populations are being moved into less-than-suitable territories, increasing rodent exposure to the human settlements that spread LASV [43]. Additionally, cross-border travel has grown during the past ten years, raising the possibility of LASV infection's spread between endemic and non-endemic nations [44].

6.3. Public health systems

The fever's unchecked development and spread over West African regions were primarily attributable to the failure of public health initiatives and the weak public health infrastructure. An effective health education, surveillance system, hospital infection prevention and control, risk communication, public health policies and laws, routined and supplemental immunizations, and epidemic readiness and response are the key elements of an ideal public health system [45].

6.4. Climate and Environment

Mastomys natalensis rodents reproduce throughout the year, but their fertility rate is highest in the wet season. An increase in rodent reproduction is facilitated by favorable environmental factors such as early rain, prolonged rainfall, and more vegetation cover. In West African nations where Lassa fever outbreaks have been observed, seasonal dynamics play a vital role in the onset and transmission of the disease. The *natalensis mastomys* rodents are known to prefer the grain crops that are typically farmed by subsistence farmers in remote West African villages. The rodents' forage for

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grains has made regular interaction of farmers with rodents and their bodily fluids /excreta that gets dumped on the agricultural products [46].

6.5. Social factors

It has been observed that human activities also play a vital role in spreading the Lassa virus. Activities such as hunting and deforestation increase rodent migration to human households for food and shelter, thus spreading infections. LASV infections are also influenced by land-use practices and demographic factors, including age, occupation, education, and sex-related exposure risk [47]. The use of herbicides on farmlands, the burning of grasslands to prepare them for planting, soil exploitation, wetlands cultivation, rodent control, and other practices have all contributed to the frequent near encounters of the target rodents with susceptible people. These interactions cause LASV discharge from the reservoirs to humans, causing infections [48].

6.6. Effects of Civil War and Conflicts

Between 1991 and 2002, a horrific ten-year civil conflict-ravaged Sierra Leone. Healthcare facilities were demolished, and health personnel's ongoing training ended. Lassa fever cases were either missed or discovered too late because of a negative impact on the disease surveillance system. The breakdown of the nation's health infrastructure, infection prevention and control procedures, and disease management programs all contributed to the spread of LASV upon its reemergence [43]. Many years after it was initially isolated in the nation, Lassa fever reappeared due to the post-conflict period [49]. A steadily enhanced public health system could have influenced the detection and subsequent resurgence of Lassa fever cases in the nation in the postwar era. A more effective surveillance system results in the detection of issues that otherwise would not have been. Despite the prospect of this, a precarious health system was undermined by the war and the postwar period. During the Biafra civil war in the late 1960s, it was evident how conflicts influenced the development of (LHF). According to the research on LASV nucleoprotein sequences, Nigeria's viral population's diversity fell between 1967 and 1970 due to the civil war before stabilizing over the past 25 years [50]. This data supports the hypothesis that violence and war contribute to establishing and spreading Lassa disease.

6.7. COVID-19 Pandemic influence

The epidemiological pattern of (LHF) from 2016 to 2022 is comparable. Compared to other years' peak seasons for (LHF) infection in Nigeria, the COVID-19 pandemic saw the most prominent peak in (LHF) condition. The effect of the COVID-19 infection on the host's immune response to other viral diseases, especially the VHFs, may help to explain this. The macrophages and dendritic cells included in the myeloid cells are the primary targets of the (LHF) virus. Although dendritic cells (DC) migrate to the lymph nodes, the LASV attack DC in an undeveloped and inactive form. The more substantial disruption of antigen-presenting cells (APCs) function by LASV compared to COVID-19 might be related to the lack of adaptive immune responses in lethal LHF. When a virus is first detected in the body, the human innate immune system responds by producing DCs to boost the activities of co-stimulatory molecules. Interferons (IFNs) for macrophages are needed for antigen presentation and boosting T-cell responses. Numerous strategies that vertebrate viruses have designed to evade immune responses are evidence of the significance of these defenses against viral attacks [51]. For instance, the (LHF) virus suppresses IFN by thwarting viral RNA sensing, which inhibits infected DCs from maturing. SARS CoV-2 innate immune system evasion and destabilizing strategies are thought to open the door for future viral infections such as LASV [52]. The Factors contributing to the re-emergence of Lassa Fever epidemics are mentioned in Figure 2.

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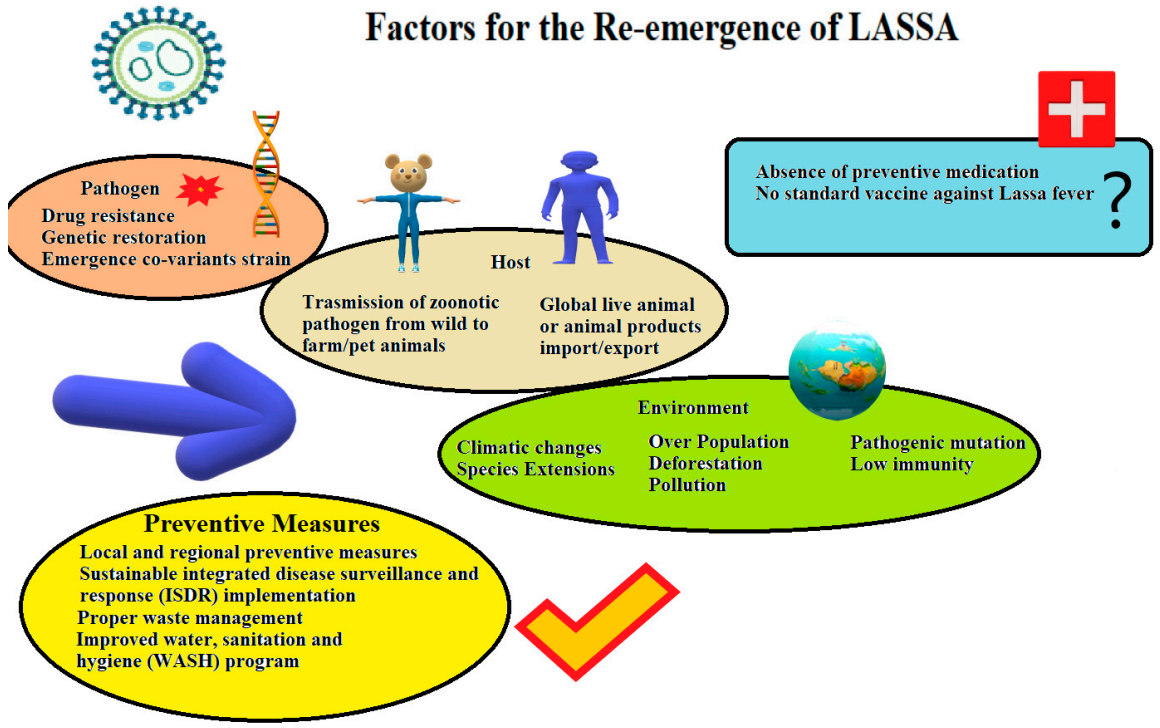

Figure 2. Factors contributing to re-emergence of Lassa Fever epidemics.

7. Preventive measures (pre-clinical, clinical trials, Measures and vaccines, medication, and vaccines)

Lassa fever ((LHF)) is endemic in western Africa, including Nigeria, Liberia, Guinea, and Sierra Leone [53]. The neighboring countries are also at risk as the vector lives throughout the region. Supportive care remains the primary treatment of LHF. The most promising drug for the treatment of (LHF) is ribavirin. Ribavirin is an analog of guanosine and has a virus-static activity on many viruses [54]. The conventional therapies used for the treatment are convalescent plasma and the use of drugs. The prevalent challenges faced in treating Lassa fever include the non-specific mode of disease presentation making clinical diagnosis difficult, high transmissibility rates, poor accessibility to treatment, and the surging cost of ribavirin. Moreover, it is limited to some specialized hospitals. The mechanism is explained in Figure 3. The preventive measures that should be taken care – avoiding rodents when people travel to the (LHF) endemic areas and minimizing transmission from person to person by maintaining personal hygiene. Patients with (LHF) should be isolated; the health care workers should be careful while transporting body fluids, wash their hands, and use contact and droplet precautions [55].

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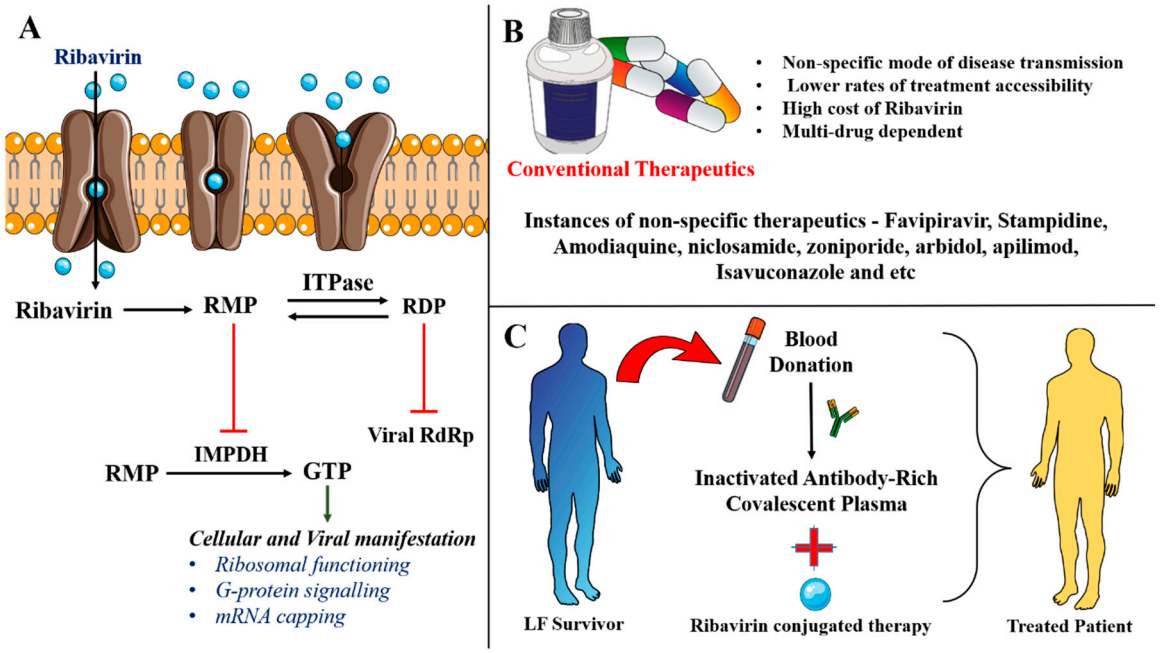

Figure 3. The mechanism of action ribavirin in Lassa infection treatment.

The convalescent plasma treatment is based on giving plasma from a previously infected and recovered patient to an actively infected patient. All the patients treated within ten days of the onset of the symptoms survived, while 75 % survived after ten days. A combination of convalescent plasma and oral or IV ribavirin was given when the levels of viremia were high, and the levels of aspartate transaminase were higher than 150 IU. Favipiravir is a nucleoside analog that acts as an inhibitor of RNA-dependent RNA polymerase in influenza viruses. It also showed a decrease in viremia. But it had side effects of nausea, transaminitis, and vomiting. Stampidine is a nucleoside derivative of d4T. It is a retroviral reverse transcriptase inhibitor showing prophylactic activity in mice. It can penetrate the central nervous system (CNS), thus having a protective role in CNS complications [56]. But, their efficacy in human subjects has yet to be determined. Amodiaquine, niclosamide, zoniporide, arbidol, and apilimod are the drugs that show potential effectiveness in inhibiting the Lassa virus [57]. Arbidol is an anti-influenza drug inhibiting viral fusion with target cells through GP-mediated and virus-cell fusion [57]. 5-ethynyl-1-b-D-ribofuranosylimidazole-4-carboxamide (EICAR) and mycophenolic acid (MPA) target the depletion of viral guanosine-5'-triphosphate (GTP). They are effective against inosine monophosphate dehydrogenase (IMPDH) and inhibit Lassa virus replication at a much lower concentration than ribavirin [58]. Isavuconazole, an anti-fungal agent (EC50 of 1.2 μM), targets stable signal peptide (SSP)-membrane fusion subunit (GP2), thus inhibiting cell-to-cell fusion of the virus [56].

There is no approved drug for the exclusive treatment of Lassa fever. Thus repurposing of FDA-approved medications will accelerate the therapeutic strategy for treating Lassa fever. Two such identified compounds are lacidipine and phenothrin, which inhibit the virus's entry by blocking the low-pH-induced membrane fusion. They also inhibited the entry of viruses, the SSP-GP2 interface being the entry target. The access is blocked, blocking the replication of the virus and its spread at an early stage [59]. Remdesvir possesses satisfactory inhibitory action against the nucleoprotein (NP) of the Lassa virus [60]. Casticinis is a botanical drug that can be used to treat Lassa fever. Bergamottin, another botanical drug, inhibited LASV entry by blocking endocytic trafficking [61]. Some of the drugs under clinical trial are tabulated below.

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Table 2. Some recent therapeutic interventions available for (LHF) along with their clinical trial IDs.

Vaccine/Drug	Clinical trial ID	Function	References
Ribavirin	NCT04285034	Cardiovascular function and pharmacokinetics and pharmacodynamics of ribavirin in Lassa fever.	[75]
INO-4500	NCT04093076	Safety, tolerability, and immunogenicity of the drug in healthy volunteers of Ghana.	[75]
rVSVΔG-LASV-GPC	NCT04794218	Evaluation of the Safety and Immunogenicity of rVSVΔG-LASV-GPC vaccine in adults in good health conditions.	[76]
MV-LASV (V182-001)	NCT04055454	We are investigating the safety, tolerability, and immunogenicity of two doses of MV-LASV.	[77]
LHF-535	NCT03993704	It assesses the safety, tolerability, and pharmacokinetics of a daily oral dose of LHF-535 administered to healthy individuals.	[52]

There currently are 21 vaccines for Lassa fever in the preclinical phases, several of which are being formed via utilizing novel technologies instead of the conventional method. Unfortunately, none of them has granted official approval for Lassa fever. The vaccines consist of inactive or killed viruses and virus-like particles, which including as DNA vaccines, [62] adenovirus-vectored vaccines, [63] recombinant vesicular measles virus, [64] vaccinia virus, [65] and ML29 MOPV/LASV live reassortant, [66] and also the recombinant stomatitis virus expressing glycoprotein (VSV-LASV-GPC) vaccine and LASSARAB, [67] Independent of the expression of the nucleoprotein, vaccines that produce the full-length Lassa virus glycoprotein protect primates against Lassa fever; In contrast, vaccines that show only the nucleoprotein or a single glycoprotein gene provides no protection. Cytotoxic T lymphocytes generally provide Lassa fever protection. At the same time, there is no correlation between pre-existing high levels of high-titer antibodies and Lassa nucleoprotein and protection from the illness. The treatment and prevention are summarised in Figure 1. The development of vaccines for treating Lassa is summarised in Figure 4.

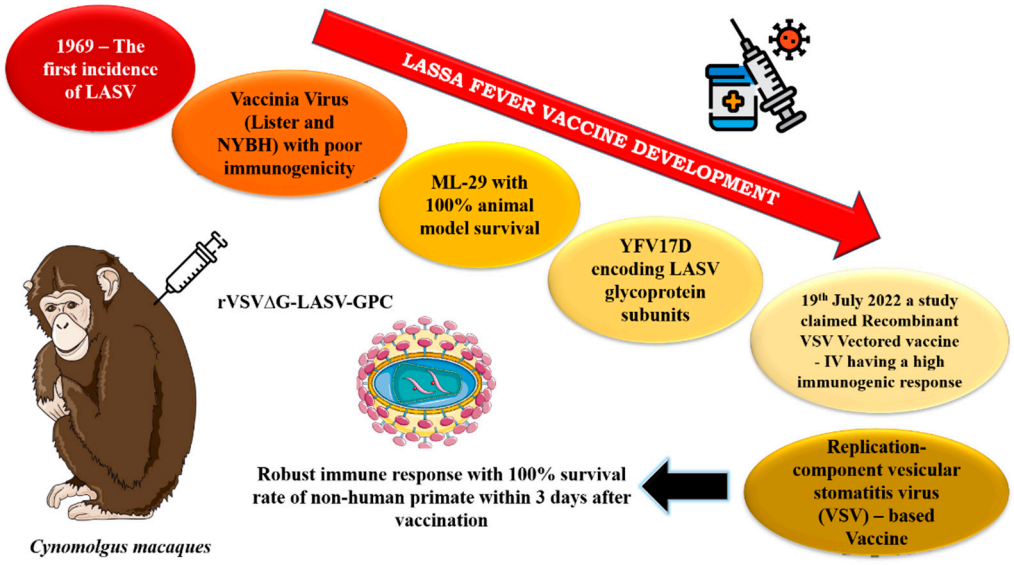

Figure 4. The chronological order of development of the Lassa vaccine.

8. Conclusions & future perspectives

Lassa fever virus outbreak, an infectious disease associated with poverty, continues to be a hazard to public health and a burden on vulnerable populations in West Africa, particularly Nigeria.

Lassa fever is severely prevalent in Nigeria and re-emerges serious repercussions and painful consequences to public health, requiring quick action. International assistance is needed to stop the current outbreak of the disease and assure the availability of vaccinations, which are the preferred treatment for Lassa fever. This would help address the issue of environmental health justice related to the Lassa virus. Despite this, vaccines have been shown to lessen patient morbidity with Lassa fever. There is always a constant need to emphasize the development of more efficient vaccinations with different action mechanisms to prevent re-emerging Lassa fever in vulnerable populations primarily. Lassa fever is seen as a disease of poverty and significantly impacts those with minimal resources; hence, sufficient funding for developing a vaccine must be crucial. We may think of the virus as neglected and endemic to West Africa. However, if the lessons from COVID-19 are any indication, then its potential future spread is still being determined by individuals. Therefore, globalization and expanding worldwide travel have been thought possible to weaponize illness. Furthermore, there is a significant amount of uncertainty regarding the role of the environment in the spread of this virus in the West African sub-region. Hence, a community, state, regional, zonal, and national public awareness campaign should be launched to educate the public on the current and potential risk factors associated with the Lassa virus. 'One Health' approach operational research system is required to understand the risk factors patterns spatial-geographically, phylogenetic in guiding evidence-based and reservoir(s) mapping, appropriate tailor-made and timely integrated plans and strategic interventions application against the disease epidemics and pandemics threats in Nigeria and the sub-Saharan Africa terrain. After all, [68] highlighted the absence of crucial resources required to manage clinical complications and the lack of suitably qualified staff as reasons why cases increased during an epidemic of Lassa fever. Moreover, a greater level of investment and coordination is required among critical stakeholders and affected communities of the Lassa fever outbreak within Nigeria, West Africa, and globally to strengthen the Lassa fever outbreak surveillance, early warning alert, preparedness, and response system [69]. Reported the transmission of the Lassa virus has social consequences besides possible exacerbation of Lassa fever. To provide a targeted management strategy, Lassa fever treatment facilities should also include teaching and training the hospitals. To stop outbreaks of Lassa fever, it is essential to improve public health surveillance, conduct more research into the creation of novel antivirals and vaccines, control rodents, and implement government policies that support rebuilding public health infrastructures and fortifying fragile health systems. To eradicate the illness globally and prevent re-emerging of Lassa fever, technical assistance, financial support, and funding across countries should be implicated internationally.

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