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NARRATIVE REVIEW

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Re-emergence of Lassa fever in Nigeria: A new challenge for public health authorities

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Abstract

The Lassa virus is an RNA virus belonging to the *Arenaviridae* family. It is responsible for Lassa fever, an acute viral zoonosis of the severe hemorrhagic fever type with manifestations of fever, muscle pain, sore throat, nausea, vomiting, and chest and abdominal pain. Lassa fever is endemic in West Africa, where the first case was reported in 1969 in Lassa, a town in Nigeria, more than 50 years ago, and it is estimated that nearly 5000 deaths occur in West Africa each year. Nigeria is one of the endemic hotspots and has experienced numerous recurrent outbreaks of Lassa fever due to the increased multiplication of the host reservoir, *Mastomys natalensis*. For the Lassa epidemics in 2022 and January 2023 alone, Nigeria accounts for a quarter of the annual deaths from this disease. Poor lifestyle and hygiene, difficulty in diagnosis due to nonspecific symptomatology, lack of effective treatment based on clinical evidence, an ineffective human immunization program combined with a health system that is not adapted or equipped to control and prevent recurrent deadly epidemics, and an outdated regional disease surveillance system in West Africa are some of the challenges that must be overcome to rapidly and effectively eradicate this disease, whose area of spread is constantly expanding as a result of the movement of populations in the context of economic and socio-cultural activities.

KEYWORDS

hemorrhagic disease, infectious disease, Lassa fever, public health, West Africa

1 | INTRODUCTION

The Lassa virus is currently endemic in various regions of West Africa. Overall, it causes an estimated two to three million infections and 10,000 deaths annually in the endemic West African regions. Nigeria has been a major target of this deadly disease.[1] Lassa fever is a viral hemorrhagic fever caused by the Lassa virus of the family *Arenaviridae*. The primary reservoir host is a rodent, *Mastomys nataliensis*, which is responsible for most of its spread.[2] The disease originated in 1969 when a nurse in Lassa, a town in Nigeria, got infected and died from it.[3]

Disease transmission occurs when a person comes in contact with a virus-infected rodent. These rodents are enzootic in various regions of Africa contaminating their houses and crops. The excreta

produced by the Mastomys directly infects mucous membranes or generates droplets that enter through the respiratory tract. Person-to-person spread is recorded in unhygienic, overcrowded areas and in hospitals where appropriate disease control measures are neglected. The clinical picture of the disease varies from mild symptoms to systemic complications indicating worse prognosis. The early manifestations of the disease include nonspecific flu-like symptoms such as fever, sore throat, cough, and malaise accompanied by gastrointestinal (GI) distress like nausea, vomiting, and diarrhea. In grave situations, the disease can progress to pulmonary edema, pleural effusion, pericardial effusion, bleeding from mucosal surfaces, signs of encephalopathy, seizures, shock, and coma. Sensorineural deafness is reported among patients as the disease advances.[4,5] The incubation period ranges from 2 to 21 days. Virus isolation through cell culture, immunofluorescence assay, complement fixation tests, enzyme-linked immunosorbent assays for LASV antigens and IgM antibodies, polymerase chain reaction (PCR), and lateral flow assays are different laboratory investigations aiding the diagnosis, while reverse transcriptase PCR being the gold standard Management of the disease is mainly supportive including fluid replacement for hemodynamic stability, dialysis in case of declining renal function and prophylactic antibiotics.[5] The specific antiviral therapy used till date is ribavirin. Ribavirin has been traditionally used for the treatment of Lassa fever. However, evidence supporting its use is insubstantial.[6] Extensive research is still ongoing to generate effective therapeutic interventions. Owing to the disease's critical complications, in-hospital mortality reaches as high as 69%.[7] With no vaccines at hand, Lassa fever poses a major health concern for the World Health Organization.

2 | LITERATURE SEARCH

A comprehensive literature search using PubMed, Google Scholar, Science Direct, and Cochrane Library was carried out. Keywords used for search strategy included “Lassa Fever,” “Lassa virus,” “Nigeria,” and “West Africa.” Articles reporting significant data on clinical picture, transmission, epidemiology, and hurdles faced while controlling Lassa fever in Nigeria were considered dating from 2000 to 2023. Exclusion criteria were based on articles irrelevant to our research objectives, not written in English language, poorly controlled trials, and animal model studies. References from the included articles were cross-checked to ensure the authenticity of the data.

2.1 | Epidemiology of Lassa fever

The first case of Lassa fever was reported in 1969 in Lassa, a town in Nigeria, from where the disease received its name.[3] The Lassa virus has experienced vast genetic mutations over time, producing seven phylogeographic lineages (I–VII), spread across the West African geographical region. Three of these lineages (I–III) have commonly affected Nigeria, in its northeastern, southern, and north-central areas, respectively. The fourth and fifth lineages are endemically located in Guinea, Sierra Leone, Liberia, Southern Mali, and the Ivory Coast, while the newly identified lineages (VI and VII) have been isolated from Nigeria and Togo.[8–13]

About 100,000–300,000 Lassa fever cases erupt each year, with almost 5000 mortalities in West Africa. Most cases occur in the dry season, usually within the December–April span.[1,8] Many outbreaks of the disease have occurred in the past, but according to the Nigeria Centre for Disease Control (NCDC), the incidence of reported cases and deaths gradually increased from 2016 onwards, with 109 laboratory-confirmed cases and 119 mortalities from 29 Nigerian states. In 2017, the number of confirmed cases rose to 322, with 70% of cases from only 3 out of 29 Nigerian states (Edo, Ondo, and Taraba). In 2018–19, the number of cases and fatalities surged significantly (20%–30% case fatality rate), with more than 80% of cases arising from the states of Edo, Ondo, Ebonyi, and Taraba. In 2020, amidst the Coronavirus pandemic, the cases uncontrollably increased to 1189 laboratory-confirmed cases with 244 deaths. Throughout the years, the predominantly affected age group was between 20 and 30 years.[14–17]

In 2021, a surprising decline was witnessed in the number of cases, as 510 patients in 17 states were confirmed to have Lassa fever. With 102 mortalities, a case fatality rate (CFR) of 20% was also reported to be reduced at the end of the year.[18] This difference in numbers may be attributed to the challenging Coronavirus Disease 2019 (COVID-19) pandemic, leading the healthcare authorities to prioritize the control of COVID-19 over Lassa fever. At times, the clinical picture of both infections would make the diagnosis more confusing and reporting of cases difficult.

The 2022 outbreak resulted in 1067 confirmed cases and 189 confirmed fatalities from 27 states, with the case-fatality ratio recorded as 17.7%. The Ondo, Edo, and Bauchi states produced 72% of all the annual cases.[19] As of March 2023, the cases are continuously rising, with 784 confirmed and 142 deaths so far.[20]

2.2 | Challenges and hurdles

Rats constitute the primary host reservoir of the Lassa virus. Agricultural and living practices in Nigeria make human contact with infected rats or their products inevitable. Food stuff and eatables are not properly covered, increasing their susceptibility to being contaminated with rats' excreta. Rats are also utilized as food. Some traditions involve consuming bathing water from corpses.[21] These habits play a crucial role in the continued transmission of the Lassa virus.

Lassa fever does not have distinct symptoms. Thus, the clinical presentation of Lassa fever has overlapping signs and symptoms with other viral infections that are endemic in the same region. Often, the disease gets misdiagnosed as malaria. Accurate and timely diagnosis can be challenging, requiring virus isolation through PCR-based assays. These kinds of modern investigations are not always available

in all endemic areas of Nigeria. Also, the vast genetic variation of LASV leads to primer probe failures and false negative results.[2]

Currently, there are not many evidence-based treatment options in the market. Ribavirin and supportive therapy constitute the mainstay of patient care. Moreover, the use of Ribavirin is still under study. Research indicates that ribavirin effectively reduces mortality for patients with elevated aspartate transaminase (AST) in Lassa fever. However, it might have negative outcomes in patients who do not have raised transaminases.[22] This puts a serious limitation on the use of Ribavirin for all cases of Lassa fever. Vaccines have proven to be an effective method for disease control and prevention. Unfortunately, no vaccines for LASV have been available for human use up till now. Trials are underway to manufacture safe and cost-effective vaccines for the disease. However, progress has been slow.[23]

Integrated disease surveillance and response (IDSR) was launched in the African region in 1998. Before this, only disease-specific control programs were active. Unusual disease manifestations such as hemorrhagic Lassa fever and common flu-like symptoms remained unnoticed through this system. This led to increased outbreaks and mortality from Lassa fever in West Africa, especially Nigeria.[24]

The public health system in Nigeria is not fully equipped with disease prevention protocols. This gave rise to continued viral transmission among healthcare workers during recent outbreaks. Lack of proper sterilization and disinfection, reuse of needles, and contact with infected fluids were found to be key contributors in this regard.[25]

Nigeria and the surrounding areas of West Africa have been the center of war and social conflicts. Where there is war, there is population dispersion. Overcrowded camps and the settlement of refugees from widespread regions made conditions ideal for Lassa virus propagation. Studies have shown more incidence of outbreaks in the refugee settlement areas.[24]

2.3 | Recommendations

Given the major risk to public health that Lassa fever represents, particularly because of its great capacity for rapid propagation, and the repeated epidemics that it causes, which can evolve on a large scale; this requires the implementation of control, contamination risk management, and prevention measures on a large scale throughout the Nigerian territory. The impact of an epidemic on social and economic activities is considerable and requires better preparation and strengthening of the health system, which has already been severely shaken by the various epidemics the country has faced. With the ever-increasing number of Lassa fever cases each year, the increased surveillance and diagnostic tests for suspicion and confirmation must be monitored to estimate the maximum incidence of cases each year.[26]

NCDC should work with local public health agencies that are in direct contact with populations in the endemic areas to ensure control of the epidemic. Health risk communication should be encouraged through awareness campaigns in print, digital, and social media, especially in states that are heavily affected by the disease. The support of health authorities and partners across the country at the beginning of the epidemic season significantly contributes to the national eradication plan.

The NCDC advises the adoption of appropriate sanitary measures, proper waste disposal practices, and safe storage of grain and kitchen items to protect against rodent reservoirs. Rat traps and rodenticides should be used routinely, and cracks and holes in house walls should be properly sealed to control the intrusion of Mastomys rat species that spread the disease.

Within health facilities, the training of qualified personnel in the management of confirmed cases of Lassa fever, and the establishment of clear guidelines as well as techniques to enable surveillance, data collection, and drawing up schemes on the diagnosis and management of Lassa fever cases are all important. Suspected cases and contact cases should be reported and documented by health personnel to the regional disease surveillance officers to investigate a possible resurgence of cases and to implement health contingency plans.

Health personnel should be advised to pay special attention when a patient presents with a non-malarial febrile illness, as the symptoms of Lassa fever and malaria overlap. The tools required for blood sample collection and storage should be identified in addition to transportation requirements to reduce the health risk of exposure. Case management requirements, including ribavirin injections and prophylactic tablets, should be generalized. The infection control department should be alerted immediately if a healthcare worker is infected with the disease. Foreign travelers are advised to read the health risk and prevention guidelines before traveling to endemic areas of Nigeria.[27–29]

Effective and long-lasting prevention and protection against the virus will be achieved through vaccines. Although there is currently no approved vaccine for the effective management of Lassa fever, vaccination is the most feasible control measure. This vaccination policy can be implemented rapidly in the most affected areas because they are well known while continuing to encourage clinical trials of promising vaccines. The availability of a potential vaccine may allow international travelers to conduct short-term pre-exposure prophylaxis for Lassa fever endemic areas. The Nigerian Ministry of Health should focus on strengthening prevention strategies and providing rapid care facilities to overcome the Lassa epidemic.

3 | CONCLUSION

The recent Lassa fever outbreak has exposed a deep-rooted mismanagement of the health care system and public safety sectors of Nigeria. The population most affected belongs to substandard living conditions and questionable hygiene practices. Amidst these overlying issues, social awareness should be raised to ensure preparedness to combat such outbreaks and health risks. Clinicians

should keep an update of disease surveillance reporting and management guidelines to efficiently and effectively curb this outbreak. There is a need to ensure preparedness to respond to the epidemic and other public health events. Regular sensitization of clinicians on disease surveillance and adherence to management protocols by health care personnel, empowerment of health facilities with a rapid and effective diagnosis of Lassa fever by ensuring that a national or state-level health system can lead the action plan proposed in this work.

AUTHOR CONTRIBUTIONS

Aroma Naeem: Validation; writing—original draft; writing—review and editing. **Shafaq Zahid**: Data curation; funding acquisition; writing—original draft; writing—review and editing. **Muhammad Hassan Hafeez**: Supervision; writing—original draft; writing—review and editing. **Arifa Bibi**: Investigation; writing—original draft; writing—review and editing. **Shehroze Tabassum**: Project administration; writing—original draft; writing—review and editing. **Aymar Akilimali**: Conceptualization; project administration; supervision; writing—original draft; writing—review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Not applicable.

TRANSPARENCY STATEMENT

The lead author, Aymar Akilimali, affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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