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Systematic Review

An X-ray of Unabated Prevention and Control of Lassa Fever Epidemic Outbreak in Nigeria: Challenges, Risk Factors, Causes, and Public Health Consequences

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Received: July 24, 2025; **Published:** August 26, 2025

Abstract

Introduction: Lassa fever is a major public health concern in Nigeria, and due to the potential for rapid dissemination, strong control and prevention strategies are crucial. The WHO recommends improved food storage, environmental sanitation practices, and early detection and treatment to reduce fatality and improve survival rates. However, despite the implementation of various interventions in Nigeria, the disease remains a persistent threat to public health, and demands urgent attention. This systematic review aims to provide a comprehensive examination of the current epidemiology and risk factors of Lassa fever, as well as the ongoing efforts to prevent and control outbreaks in Nigeria. It highlights the challenges of current prevention and control strategies and identifies crucial areas for improvement.

Materials and Methodology: This is a systematic review that focuses on published research articles about Lassa fever epidemiology in Nigeria and the risk factors contributing to outbreaks. It also reviews the control and prevention measures currently in place and the challenges faced while controlling Lassa fever in Nigeria. Studies reviewed comprise of cross-sectional, prospective, longitudinal and observational studies. The review follows a systematic approach, analyzing peer-reviewed articles and online publications from various databases, using search keywords relevant to Lassa fever.

Results: The findings in this study highlight the endemicity of Lassa fever in various parts of Nigeria, revealing an increasing trend in the number of affected states, suspected cases, confirmed cases, health workers affected, and the case fatality ratio over the years. The study also illustrates how the disease is influenced by factors including temperature, humidity, and seasonality, as well as poor housing conditions, poor sanitation and hygiene, unsafe food processing and storage, hunting and consumption of rodents, inadequate healthcare infrastructure, indiscriminate disposal of hospital waste, and the lack of personal protective equipment for healthcare workers. Furthermore, the study highlights the current strategy employed to control, monitor, and manage the ongoing outbreaks in the country. Finally, it pinpoints factors such as poverty, community lifestyle, socio-cultural practices, illiteracy, poor public awareness and education, misdiagnosis, weak healthcare infrastructure, shortage of medical practitioners, government negligence, weak surveillance, lack of proper reporting, and social unrest as key factors that hinder the implementation of control and preventive measures.

Conclusion and Recommendation: Lassa fever in Nigeria continues to resurface, highlighting the limitations of current measures. Effective management requires a multifaceted approach, with sustainable leadership commitment, crucial for strengthening integrated outbreak surveillance and intervention. Also, promoting economic growth, enhancing hygiene, and prioritizing research will play key roles in long-term disease control.

Keywords: *Lassa Fever; Nigeria; Prevention; Control; Outbreak; Public Health Impact*

Introduction

Lassa fever (LF) is an acute viral hemorrhagic illness caused by the Lassa virus (LASV) which is classified within the Arenaviridae family, a family of negative-sense, single-stranded RNA viruses [1,2]. Endemic to various parts of West Africa, including Nigeria, Benin, Côte d'Ivoire, Mali, Sierra Leone, Guinea, and Liberia. LASV remains a persistent threat to public health in Nigeria, which bears the highest burden of Lassa fever in sub-Saharan Africa, with records documenting community and healthcare-associated transmissions of the disease [3-5]. This trend has been accompanied by an expanding geographic distribution within the country [6,7].

Transmission primarily occurs through exposure to urine and feces of the *Mastomys natalensis* rodent, a prevalent species in sub-Saharan Africa acting as a reservoir for the virus [8,9]. Human-to-human transmission, mainly in healthcare settings, has also been reported [10]. The clinical manifestation of the disease is nonspecific and includes fever, fatigue, hemorrhaging, gastrointestinal symptoms, respiratory symptoms (cough, chest pain, and dyspnea), and neurologic symptoms (disorientation, seizures, and unconsciousness) [11]. Patients hospitalized for severe LF have an observed case-fatality rate (CFR) ranging from 15% to 50% [12,13]. Nonetheless, around 80% of illnesses in humans are thought to have mild or no symptoms, and thus go undetected [13].

The disease is most prevalent in rural areas with high rodent populations, attributed to poor living standards, sanitation practices and daily environmental lifestyle common in high-risk areas [14]. The cyclical nature of its outbreaks, coupled with the potential for rapid dissemination, highlights the importance of robust prevention and control measures. Due to the absence of vaccine against the virus and the impractical control of the rodent host population, the World Health Organization (WHO) recommends preventive and control strategies for Lassa fever, including improved sanitation, proper food storage and environmental sanitation [15]. Early detection and treatment of LF are recommended to reduce fatality rates and improve survival rates. Health professionals dealing with infected persons must use approved safety measures to avoid contact with body fluids [15]. Also, enlightenment and awareness of the public on risk factors associated with spread of disease is important for prevention [16]. However, despite the implementation of various interventions, the disease remains a persistent threat to public health in Nigeria, presenting a complex web of challenges that demand urgent attention.

This review aims to provide a comprehensive examination of the ongoing efforts to prevent and control Lassa fever outbreaks in Nigeria. We aim to shed light on crucial areas for improvement by examining the complex issues healthcare systems face, the interplay of risk factors influencing disease transmission, and the far-reaching public health consequences of Lassa fever epidemics. In order to lessen the effects of upcoming outbreaks, this study also emphasizes how urgent it is to close the gaps in the prevention and control methods already in place. Through the synthesis of existing research, identification of critical areas requiring intervention, and formulation of feasible recommendations, our aim is to make a meaningful contribution to the joint effort to protect public health and mitigate the prevalence of Lassa fever in Nigeria and other regions.

Materials and Methodology

Study approach

The study employs a systematic review methodology, which involves a thorough review of previously published research articles to analyse and synthesize relevant information that may be added to a body of work to create another interesting body of knowledge for the

benefit of the scientific community. A systematic review, according to Denyer., *et al.* [17], is a scientific analytical methodology that collects previously published studies with the goal of evaluating, analyzing, and synthesizing the findings, then reports them in a way that enables clear comprehension and conclusions to be drawn on topic of discourse [17].

Search strategy

The search strategy used in the development of this article involves the combination of relevant keywords employed in the search of databases such as ResearchGate, Lancet, PubMed, Google Scholar, and Science Direct. Also, various online articles published from reputable and verifiable websites such as WHO were reviewed in the course of writing this article. Google searches of certain important keywords relevant to the article were also carried out to gain generalized knowledge on the topic, as well as search for useful articles for review. Some of the keywords used in searching for information on the topic are "Lassa fever", "outbreak of Lassa fever", "epidemiology of Lassa fever", "risk factors of Lassa fever", "control measures of Lassa fever", "prevention of Lassa fever", and "public health impact of Lassa fever".

Inclusion criteria

Several published articles were encountered during the writing of this article, but only those that were relevant to the topic of discourse were reviewed; those that did not fit these requirements were not used, and only English-language publications were taken into consideration.

Exclusion criteria

Articles that did not address the subject matter under discussion were removed. Additionally, publications published in languages other than English were not considered during the selection process, and finally, information from sources that lacked credible references supported by evidence was not taken into account during the systematic selection and review process.

Background knowledge

Brief history of Lassa fever outbreaks

Genetic dating suggests a longstanding occurrence of zoonotic transmissions of LASV to humans, spanning decades [18]. This phenomenon aligns with molecular clock estimates, which propose that Lassa virus potentially evolved from an ancestral stock approximately 500-1000 years ago [19]. The wide geographic distribution of Lassa viruses, along with various genotypic lineages being associated with human disease, underscores its antiquity as a disease that has been historically overlooked or misidentified in medical contexts [20]. Andersen., *et al*. [18] utilized molecular dating techniques to trace the origins of extant LASV strains back to modern-day Nigeria, with indications of their spread into neighboring West African countries over the past several hundred years, supporting its ancient lineage.

It was first described in West Africa in the 1950s, however, it was not until 1969 that the first patient with LF was described in the town of Lassa in present day Borno state, northern Nigeria [21]. The patient was a missionary nurse infected while working in a rural clinic near Lassa, Nigeria. She developed fever, back pain, sore throat with ulcers, leukopenia, swelling of the neck and renal failure. By the time evacuation by road and light plane to Bingham Memorial Hospital in Jos was arranged, she was severely ill with respiratory distress, petechial rash, hypotension, obtundation, and convulsions. Despite intensive care, she died in 24 hours, 6 days after onset. Gross autopsy showed internal hemorrhages but was otherwise uninformative [20].

In Jos, two additional nurses were infected and died. A third nurse survived infection after being transported to New York City [22]. The nurse had a complicated recovery over nine weeks. Blood samples from the infected nurses were analyzed at Yale University, where LASV was first isolated. The isolate was designated as the type strain. Two Yale researchers were infected with LASV during these initial studies.

Tragically, one of these infections was fatal. The surviving virologist Dr Jordi Casals received blood donated from the nurse as passive immunotherapy [23-25]. Frame., *et al*. [21] published the first report, naming the disease Lassa fever after the location of the original case.

Not long after it was discovered, in January 1970, the Lassa virus struck two mission hospitals located in Jos, Nigeria. There were 28 cases in this nosocomial outbreak, 16 of which were hospitalized, and 13 of which were fatal (46%). Don Carey and a group from the Rockefeller Foundation Virus Research Laboratory in Ibadan looked into the outbreak [26]. A more thorough description of the disease's pathology and clinical characteristics was made possible by the outbreak [27,28].

While the Lassa rodent host was yet to be identified, the mechanisms causing persistent infection and human exposures were also poorly understood. In 1972, during an outbreak of LF in Sierra Leone's Eastern Province, LASV was initially isolated from peri-domestic rats. The virus was identified in the natal multimammate mouse (*Mastomys natalensis*) that was found in the homes, yards, and fields of the residents [29,30]. Between 1973 and 1976, there were more Lassa fever epidemics in Sierra Leone and Nigeria [31,32]. These incidents, along with serological studies and surveillance of missionaries, demonstrated the widespread distribution of the Lassa virus in West Africa [33,34].

Throughout the 1980s and 1990s, Lassa fever gained recognition as a significant public health threat in West Africa. In Nigeria, there were no reported outbreaks between 1981 and 1988, but from 1998 there was no year without an outbreak [35], causing significant morbidity and mortality, particularly in resource-constrained settings. By early 2000s, information gathered from Epidemiology Division of the Federal Ministry of Health in Nigeria, stated that Lassa fever has been reported in more than 23 of the 36 States in which Ebonyi, Edo, Nassarawa and Plateau States are the worst hit repeatedly of all States in which Lassa fever cases have been reported [11,36].

Current situation and trends of Lassa fever outbreaks in Nigeria

An international conference was held in January 2019 to commemorate the 50th anniversary of the first report on LF [37]. The NCDC reports that although there have been numerous outbreaks of the disease in the past, from 2016 onwards there was a progressive increase in the number of reported cases and deaths, with 109 laboratory-confirmed cases and 119 fatalities from 23 states in Nigeria. Prior to 2016, Nigeria had weak laboratory diagnostic capabilities for Lassa fever and attempts at describing Lassa fever were limited by a lack of robust, nationwide, case-based data [4]. Among the few specialized Lassa fever centers in the West African region, the diagnosis was primarily jointly supported in the laboratories of the Lagos University Teaching Hospital (LUTH), Irrua Specialist Teaching Hospital (ISTH), Nigeria, and the Institute of Lassa Fever Research and Control (ILFR&C).

The number of confirmed cases increased to 322 in 2017, with only three states Edo, Ondo, and Taraba, representing 70% of the total number of cases. In 2018, the Surveillance Outbreak Response Management and Analysis System (SORMAS), an electronic case-based surveillance system, was utilized by the states with cooperation from the NCDC to begin thorough recording of Lassa fever. These initiatives enhanced the surveillance of Lassa fever, leading to a rise in cases reported and the world's largest outbreak ever observed. The outbreak included 23 states (of the 36 states in Nigeria including the Federal Capital Territory) and had an increased incidence and geographic distribution [38].

During the 2020 coronavirus pandemic with attention shifting away from Lassa fever, laboratory-confirmed cases increased to 1181 with 244 fatalities. The age range most frequently impacted throughout the years was 20 to 30 years old [39,40]. In 2021, the number of cases declined surprisingly, with 510 patients in 17 states confirmed to have Lassa fever. After the year, the case fatality rate (CFR) also decreased by 20%, with 102 fatalities [41]. The drop in reported numbers for 2021 is likely due to either the strain on the surveillance system from the massive outbreaks in 2018 and 2019 or the diversion of surveillance and response resources to other significant challenges, such as the COVID-19 pandemic. Alternatively, it may indicate a genuine reduction in cases [42]. The 2022 outbreak resulted in 1067 confirmed cases and 189 confirmed fatalities from 27 states, with the case-fatality ratio recorded as 17.7%. Ondo, Edo, and Bauchi states produced 72% of all the annual cases [43].

In 2023, the cases continuously rose, with 1270 confirmed cases and 227 deaths [44]. Twenty (28) States recorded at least one confirmed case with Ondo, Edo, and Bauchi contributing to 76% of all cases. The NCDC noted that the challenges of containing the disease arose from several factors, including the late presentation of cases, which led to an increase in the CFR. Additionally, poor health-seeking behavior due to the high cost of treatment and clinical management of Lassa fever and also the poor environmental sanitation conditions and a lack of awareness about the disease in high-burden communities [44]. As of April 2024 (week 17), the cases are continuously rising, with 857 confirmed and 157 deaths in 28 states across the country so far [45]. Ondo, Edo, and Bauchi still contributed the highest burden, accounting for 63% of all confirmed cases. The NCDC also reported an increase in the number of suspected cases in 2024 compared to that reported for the same period in 2023 [45].

Year	States Affected	Suspected Cases	Confirmed cases	Health workers affected	Death (Confirmed cases)	Case fatality rate
2014	13	989	110		36	3.64
2015	15	430	25	-	40	9.3
2016	23	921	109	10	119	12.9
2017	19	1022	322	-	127	28.6
2018	23	3498	633	45	191	27
2019	23	5057	833	20	174	20.9
2020	27	6732	1181	47	244	20.7
2021	17	4654	510	10	102	20
2022	27	8202	1067	63	189	17.7
2023	28	9155	1270	56	227	17.9

Table 1: *Epidemiology of Lassa fever from 2014-2024 (April, Week 17) according to the Nigeria centre for disease control and prevention (Lassa Fever Situation Report).*

States affected, suspected and confirmed cases, number of health workers affected, deaths and case fatality rate in Nigeria from 2014 - April, 2024. Source [Nigerian Centre for Disease Control and Prevention].

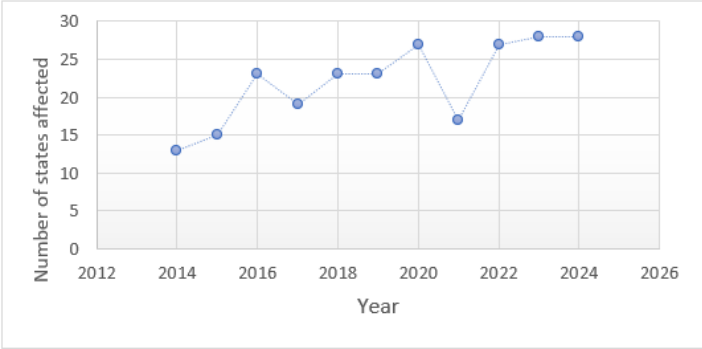

Figure 1: *Trends in number of states affected by Lassa fever from 2014-April 2024 (Week 17).*

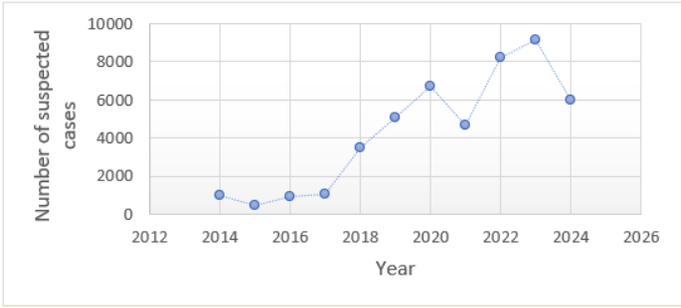

Figure 2: *Trends in number of suspected cases of Lassa fever from 2014-April 2024 (Week 17).*

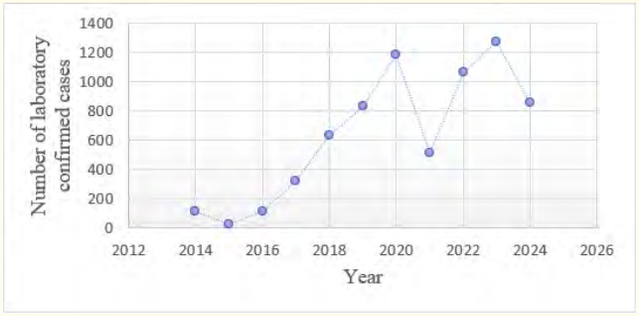

Figure 3: *Trends in number of laboratory confirmed cases of Lassa fever from 2014-April 2024 (Week 17).*

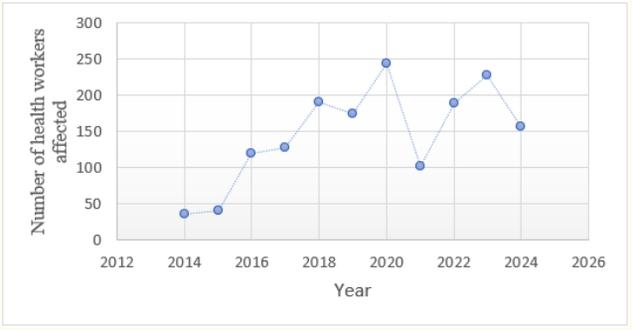

Figure 4: *Trends in number of health workers affected by Lassa fever from 2014-April 2024 (Week 17).*

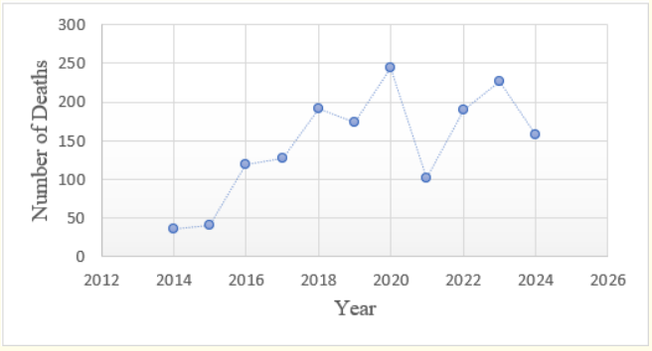

Figure 5: *Trends in number of death (Confirmed cases) from Lassa fever from 2014-April 2024 (Week 17).*

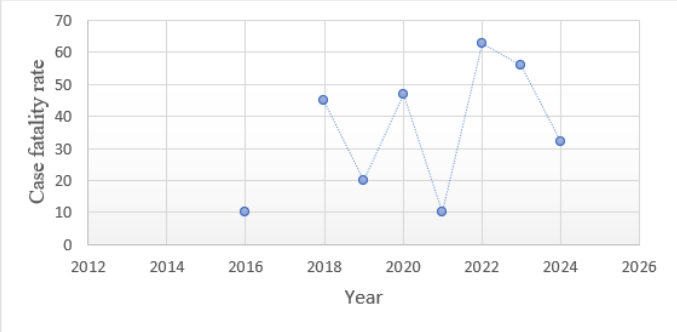

Figure 6: *Trends in case fatality rate (CFR) of Lassa fever from 2014-April 2024 (Week 17).*

Unabated emerging and re-emerging risk factors of Lassa fever

The risk factors for Lassa fever spread include environmental and ecological aspects, such as rodent populations that act as natural virus reservoirs, and human behaviors that increase exposure to these rodents [9,46]. Socioeconomic factors, including educational level, occupation, and income, influence the spread of Lassa fever due to a lack of amenities, malnutrition, unclean environments, low standards of living, insufficient health facilities, lack of clean water sources, and poor personal hygiene [47]. Seasonal variations also impact interactions between rodents and humans [48]. Furthermore, inadequate infrastructure for public health and low levels of disease knowledge raise the risk of outbreaks [49,50]. Addressing these factors is crucial for developing effective strategies to prevent and control Lassa fever.

Environmental factors: Temperature, humidity, and seasonality are key environmental predictors of Lassa fever transmission [48,51]. Lassa fever cases in Nigeria typically peak during the dry season [48,51], likely due to changes in human-rodent interactions between the rainy and dry seasons, which influence Lassa fever transmission. During the dry season, rodents migrate from their natural habitats to human settlements in search of food and shelter. These settlements, especially those with poor sanitation, provide ideal breeding grounds for rodents, which persist even after the rains begin. Habitat suitability varies across Nigeria, with the coastal south, consisting mostly of mangroves and rainforests, being unsuitable for *M. natalensis* habitation. In contrast, agricultural practices in the northern regions may drive rodent movement toward human settlements in response to climatic changes, potentially increasing LASV incidence [52].

Furthermore, LASV exhibits a seasonal pattern in its incidence, with a spike in reported cases typically occurring in the early months of the year, exceeding the rates observed during the rest of the year. Similar to other arenaviruses, LASV is more sensitive to high temperatures and low humidity than its rodent host [53]. Stephenson., *et al*. [54] found that the rate of nosocomial Lassa fever outbreaks is significantly higher during the dry season than the wet season. This increase is attributed to the higher survival rate of the virus in hot weather when aerosolized with *M. natalensis* urine. During the dry season, higher temperatures and increased relative humidity can cause microaerosols to form from dust on floors, enhancing virus transmission. Additionally, Ogbu., *et al*. [55] noted that the virus could be transported from one endemic region to a non-endemic one during the incubation period, potentially causing an outbreak at any time of the year, irrespective of the season. Understanding these seasonal patterns is crucial for predicting future outbreaks and identifying areas for public health interventions.

Housing conditions: Poor environmental sanitation, inadequate housing structures, and rodent infestations contribute to Lassa fever transmission [46]. Housing quality is a significant factor in Lassa fever transmission and in deploying effective control mechanisms [9,56]. Gbakeji., *et al*. [56] identified aspects of housing quality such as house fittings, screenings, amenities, housekeeping, and surroundings that

can attract or repel rodents implicated in Lassa fever transmission, highlighting a major challenge in controlling vector-borne diseases. According to Oboratare., *et al*. [57], settlements with more Lassa fever cases had poorer hygiene compared to those with fewer cases. This aligns with findings by Bonner., *et al*. [58], who noted that the poor state of houses increases the risk of rodent infestation and Lassa virus transmission in the immediate surroundings of homes. Although, a cross-sectional study among 247 houses in two settlements in Ekpoma, which examined the roles of housing quality and hygiene in Lassa fever transmission, showed that poor hygiene, rather than housing quality, was significantly associated with Lassa fever transmission [59].

According to Gbakeji., *et al*. [56] and Ogwu [60], most household wastes consist of kitchen leftovers and spoiled food items. When proper disposal methods are not available, these wastes become food sources for vectors, particularly rats. In many regions of Nigeria, waste dumpsites are located close to residential areas, leading to an increase in vector populations and a subsequent rise in zoonotic diseases. In rural areas, practices such as storing firewood in heaps behind households and disposing of organic household waste in nearby areas for composting attract vectors like flies and rodents [52]. Additionally, surrounding shrubs, home gardens, and seasonal fruit trees provide shelter for rodent species. Consequently, poor sanitation and hygiene can significantly increase the risk of rat infestations, thereby facilitating the transmission of the Lassa fever virus to individuals whose homes are infested, as well as to the surrounding environment [52]. Alenoghena and Omuemu [61] emphasized that poor housing conditions are a serious concern, as they may undermine all other efforts to control repeated Lassa fever outbreaks.

Agricultural practices: Changing farming practices and unsafe food processing and storage are common risk factors associated with the spread of Lassa fever [62]. In Nigeria, commercial agriculture is uncommon as most of the population engages in subsistence farming practices, primarily in rural areas. These practices often lead to significant deforestation and habitat loss [63-65]. Due to the lack of mechanized tools, farmers commonly use the slash-and-burn method to clear forests for agricultural purposes. During the preparatory period, which involves bush clearing and burning, especially during the dry season (November-April), the habitats and food sources of rodents are destroyed, causing them to move closer to or into human residences in search of new habitats and food sources [48]. This movement of rodents and other animal species from forested areas to human settlements, driven by anthropogenic activities, poses significant dangers [48], and this could also be responsible for prevalent outbreaks recorded during the dry season in some parts of Nigeria [66].

Inter-border communal trade of farm produce among local communities, often characterized by overcrowding and poor sanitation, can facilitate the spread of Lassa fever in areas with limited awareness [67]. A common practice that promotes contamination and transmission of the infection is the open drying of farm products, occasionally along roadsides [62]. In rural regions, semi-processed foods are frequently spread along walk paths to dry, attracting rodents and increasing the risk of contamination with rat excreta or urine [67]. This practice is not limited to Nigeria but is also common among rural farmers in other West African countries [68]. Therefore, the prevention and control of Lassa fever at the grassroots level largely depend on implementing good community hygiene measures that discourage contact with rats and their urine or droppings [69].

Food storage: A significant contributing factor to the spread of Lassa fever is improper food storage; local farmers typically lack access to rodent-proof storage containers. Food is often stored in baskets and other containers lacking lids and coverings [60]. This makes the containers ideal prey for rat populations that forage for food, raising the risk of contracting LASV infections. This is not exclusive to farms; it also occurs in homes infested with rats where food is left out exposed or improperly reheated after it has been left out in the cold. Research has shown that improper food handling procedures, particularly when handling food in non-airtight containers, are linked to an increased risk of LASV [70,71]. A study conducted in Edo state by Ben-Enukora., *et al*. [72], noted that high-risk practices like consuming foods half-eaten by rodents after removing the contaminated portions can lead to Lassa fever spread.

Consumption of wild animals: The hunting and consumption of wild animals, commonly referred to as "bushmeat", has increased in recent times, contributing to the transmission of Lassa fever [73-75]. Abdullahi., *et al*. [48] noted that rodent hunters have a higher risk of exposure to Lassa virus infections. During the hunting process, hunters come into contact with the bodily fluids of rodents, particularly during slaughtering. Some hunters search for rat burrows and set them on fire to force the rodents out, while others, including farmers, set forested areas on fire, driving all animals from their natural habitats and increasing human contact with zoonotic diseases, including LASV [76,77]. Despite the risk of epidemics linked to LASV, poverty remains a significant reason for continued rodent hunting [77,78]. According to UNEP [79], wildlife is exploited globally for various purposes, including food, income (especially among the poor in developing and low-income countries), medicine, rituals, decorations, and recreation (e.g. zoos and recreational hunting). Wildlife consumption has increased over the last decade, and hunters' close contact with animals raises the risk of catching and transmitting zoonotic diseases [79].

Healthcare infrastructure and healthcare workers: Person-to-person transmission of Lassa fever can occur through direct contact with the blood or bodily fluids of infected patients, posing a significant risk to healthcare workers (HCWs). HCWs are at the highest risk of contracting and transmitting LF because of their frequent contact with infected patients and blood or body fluids [80]. These outbreaks are often attributed to a lack of strict infection control practices and the inadequate use of personal protective equipment (PPE) by HCWs [81].

Nosocomial transmission of Lassa fever in healthcare facilities represents a significant burden on the healthcare system, exacerbated by Nigeria's low-income status and ill-equipped healthcare infrastructure [49]. Effective infection prevention and control (IPC) measures in healthcare settings are crucial for controlling potential outbreaks [82]. A study by Ijarotimi., *et al*. [83] revealed that hospitals with improved IPC practices experienced minimal transmission of the Lassa virus.

Health workers in contact with patients infected at the community level are also at increased risk, especially if they do not adhere to basic infection control measures during patient care [81]. Contact with potentially contaminated surfaces without proper PPE, particularly in hospitals, is another potential transmission route for the Lassa virus [84]. Additionally, wastes generated in hospitals and diagnostic centers pose a serious risk for the spread of the Lassa virus. Infectious wastes from clinical consumables and equipment can carry microorganisms when they come into contact with bodily fluids or tissues from patients. Chemical or radioactive wastes can also potentially transmit nosocomial infections among personnel, patients, caregivers, and the environment [85]. Proper segregation and disposal of medical wastes are essential to minimize the transmission of the Lassa virus in clinical settings [52].

Current control and prevention measures of Lassa fever in Nigeria

A multifaceted strategy including monitoring, vector management, diagnostics, strengthening the healthcare system, and public awareness campaigns is needed to control Lassa fever [86]. Additionally, adherence to healthcare protocols and enhanced personal protective measures are essential components in reducing the risk of transmission [55]. 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 [87].

Since 1969, Nigeria has not implemented government intervention for Lassa disease control until 2011 when the NCDC was established [88,89]. In 2016, the NCDC developed the Viral Haemorrhagic Preparedness and Response Plan to control viral hemorrhagic fevers, including Lassa fever (LF). This comprehensive document outlined the roles of key players in Lassa fever management and defined clinical

management and control strategies. A digital surveillance system called surveillance, outbreak response management and analysis system (SORMAS) was adopted for reporting, managing, and controlling Lassa cases. SORMAS is operational in 174 local government areas in Nigeria and has significantly improved the surveillance and management of LF [89].

Following the largest outbreak of Lassa fever (LF) in 2018, the Nigeria Centre for Disease Control (NCDC) developed national guidelines for the management and control of Lassa virus (LVS) infection. This document incorporated strategies from the Viral Haemorrhagic Fever (VHF) plan as well as new control efforts such as infection prevention control (IPC) and integrated surveillance as recommended by WHO [90]. These new guidelines have significantly improved the awareness, detection, and control of LF in Nigeria. Although the burden of the disease increased over the years, the guidelines has been attributed to improved surveillance and diagnosis rather than a failure of control programs [90].

Some interventions highlighted in the NCDC 2018 annual report include the activation of Public Health Emergency Operations Centres (PHEOC) in 11 states [91-93], 14 intervention deployments in 2018, the establishment of a national first responder team (N-FIRST), and the diagnosis of LF in Kebbi State for the first time in early 2019 [89]. Other notable developments include the establishment of six national reference laboratories and other laboratory networks across the country, as well as genomic surveillance capacity provided by the Africa Centre of Excellence for Genomics of Infectious Disease (ACEGID) and other research institutes. This local genomic surveillance capacity was immensely beneficial in the early detection and control of the 2018 outbreak [94]. Also, the World Health Organization is collaborating with the Nigeria Federal Ministry of Health in the surveillance of and response to outbreaks of Lassa fever, covering contact tracing, follow-up, and community mobilization. However, more integrated and sustainable efforts are needed to effectively improve the control and prevention of LF infection.

The year 2019 marked the 50th anniversary of LF in Nigeria. The first international conference was organised by the NCDC to enable researchers to collaborate with each other and share research findings about Lassa fever with regard to what is known and where knowledge gaps still exist and to prioritise the Lassa fever research and response plan for the future [37]. Surveillance training was provided for public health officers at both national and state levels. Sensitisation to increase awareness of the disease was conducted for healthcare workers through workshops and for the general public through media such as radio, television, poster and social network services. Strengthening of laboratory capacity and sample transportation system has also facilitated disease detection and reporting through establishment of the Lassa fever laboratory network [92]. In recent years, the provision and use of personal protective equipment (PPE) for health care workers has resulted in a significant decline of confirmed LF cases among the Nigerian health care workers and the spread within hospital settings coupled with the intense effort in contact tracing [95-97].

Public health consequences of Lassa fever infection

Infection with Lassa fever can have serious health impacts on the public, especially in areas of West Africa where the disease is endemic [3-5]. High rates of morbidity and mortality from the virus frequently put further strain on already underfunded healthcare systems. Nigeria, for example, experiences outbreaks in most states, sometimes with unclear and unusual fatality profiles. Despite some progress in understanding the virus's replication pattern, Nigeria and other West African countries continue to face frequent community and nosocomial outbreaks, often resulting in significant fatalities and severe economic burdens [98].

While approximately 80% of Lassa fever infections produce minimal symptoms, the symptomatic disease can lead to severe symptoms requiring hospitalization and potentially resulting in death [99,100]. Additionally, around one-third of Lassa fever survivors develop sudden onset sensorineural hearing loss, costing Nigeria $43 million annually [101]. There is also strong suspicion that Lassa fever can cause depression and psychosis [102,103].

Additionally, Lassa fever evokes fear due to its high infectivity and the delay in diagnosis, leading to stigma from both the public and health professionals [104]. In Ebonyi State, Nigeria, a study found that about 32.2% of respondents held stigmatizing attitudes and were unlikely to accept survivors who had been successfully treated [105]. Children whose parents were infected also faced discrimination, as community members, including relatives, no longer welcomed them [11]. The stigma surrounding Lassa fever in Nigeria underscores its ongoing status as a public health threat [105].

The economic losses due to Lassa fever including direct, indirect, and opportunity costs have never been thoroughly evaluated [106]. The direct costs of Lassa fever include expenses for obtaining a hospital card, various medical investigations, hospitalization, treatment, medical supplies, and follow-up visits [107]. Treating Lassa fever patients, implementing control measures, and conducting research on the virus place a significant burden on healthcare systems and economies in affected areas [108].

The economic impact extends beyond the health sector, affecting agriculture, trade, and tourism. The cost of healthcare, loss of productivity, and trade disruptions due to the fear of outbreaks pose significant economic burdens on affected countries. Recurring outbreaks disrupt local economies, diverting resources from other essential health programs. Additionally, the risk of nosocomial transmission poses a serious threat to healthcare workers, exacerbating workforce shortages [109]. Effective public health strategies are essential to mitigate these impacts, emphasizing early detection, improved healthcare infrastructure, community education, and robust infection control measures.

Discussion

The geographic spread of Lassa fever has significantly increased in Nigeria over the past decade, with the number of affected states rising from 13 in 2014 to 28 in 2023 and 2024. This expansion is accompanied by a general upward trend in suspected cases, which peaked at 9,155 in 2023. The rise in suspected cases may be attributed to improved reporting and awareness, or it might reflect an actual increase in the disease's incidence. Confirmed cases have also surged, from 110 in 2014 to 1,270 in 2023, indicating a consistent effort in diagnostic confirmation. The number of health workers affected has varied, with the highest number recorded at 63 in 2022, highlighting the occupational risk faced by these workers and underscoring the need for proper protective measures and training. Although the case fatality rate (CFR) has fluctuated, reaching a high of 28.6% in 2017 and decreasing to 17.9% in 2023 and 18.2% in 2024, there remains a concerning rise in deaths among confirmed cases, peaking at 1,270 in 2023.

The response to this escalating crisis has been hampered by systemic challenges that limit Nigeria's ability to effectively control the spread of Lassa fever. The resurgence of Lassa disease in Nigeria is attributed to deficiencies in surveillance, delays in laboratory testing, and reduction in case management capacity due to the conversion of dedicated Lassa fever facilities into COVID-19 healthcare facilities. Factors like poverty, education, socio-cultural beliefs, and lack of technological approaches contribute to the situation. Neglect by the government has also contributed to sustaining the burden of LF in Nigeria. Additionally, suboptimal infection prevention and control procedures contribute to a high overall risk assessment and further complicate the situation. Some of the challenges of the control and prevention measures of Lassa fever are discussed below. Tackling these challenges, will play important role in improving Lassa fever prevention in Nigeria.

Viral diversity: LASV has a high genetic diversity and this makes implementing control measures extremely challenging. Seven different lineages have been identified so far [110]. The understanding of the virus is still incomplete, with several lineages only recently discovered [99,111]. The combination of high genetic diversity and insufficient characterization complicates the development of effective medical countermeasures due to variations in pathogenicity among different lineages. The prototypical strain, Josiah (lineage IV), has been utilized in numerous pre-clinical investigations; however, as demonstrated by challenge in guinea pigs, it is not always the most virulent [112]. Vaccines developed to target this strain may be less effective against other strains that are in circulation [113].

Lassa fever cannot be efficiently managed with a single strategy, like distributing medications or prophylactics in large quantities. A thorough approach is needed, beginning with in-depth genomic research to map the diversity of LASV in each endemic area. Particular attention should be paid to the characterization and sequencing of recently discovered and underrepresented lineages. Designing successful vaccinations and treatments may benefit greatly from an understanding of how various lineages change and adapt. Furthermore, to identify and track the dissemination of different lineages and ensure focused and knowledgeable control actions, it is crucial to establish strong monitoring systems in endemic and at-risk areas.

Poverty and community lifestyle: Lassa fever is a disease closely linked to poverty as the highest risk of infection occurs among the poorest in endemic countries [114]. According to the highlights of the 2022 Multidimensional Poverty Index survey, 63% of people living in Nigeria - equivalent to 133 million individuals [115]. Multidimensionally poor individuals often live in overcrowded, poorly constructed housing, which increases their exposure to rodents, the primary reservoir of the Lassa fever virus. According to Gibb., *et al*. [9] and Happi., *et al*. [89], the economic status of rural populations increases their contact with the rodent reservoir of the Lassa fever virus. Limited access to proper sanitation and waste disposal in these communities also attracts rodents, creating a higher likelihood of human contact with contaminated food or surfaces [48,89]. Rodent management is an efficient way to stop Lassa fever outbreaks and should remain a priority. Additionally, impoverished populations are more likely to engage in risky behaviors, such as consuming rodents as a food source, which further increases their vulnerability to infection [14,116,117]. The inability to afford proper healthcare or preventive measures, such as rodent-proofing homes or accessing early medical treatment, worsens the situation, making poverty a key driver in the continued incidence of Lassa fever. Preventing the spread of Lassa fever in Nigeria necessitates focused poverty-reduction measures, like: enhancing housing and sanitation in low-income neighborhoods, improving access health infrastructure in underserved and rural areas, and launching public health initiatives to increase knowledge of preventative measures.

Social-cultural practices: Some cultural beliefs and practices predispose people to Lassa fever and hinder control programs against the disease. When ill, some individuals prefer to seek help from local traditional healers rather than orthodox medical practitioners [96]. The inability to access quality medical care affects the control of LF [89]. The practice of seeking medical intervention from local traditional healers puts both traditional healers and their clients at risk of Lassa virus (LVS) infection. A classic example is the West African Ebola outbreak in Sierra Leone, which spread to Guinea through a renowned traditional healer [118]. Additionally, certain burial practices expose people to Lassa fever. These practices include bathing, shrouding, community display of the deceased, dancing on the streets with the corpse, and the traditional practice of forcefully ingesting bathing water from dead corpses. These actions increase the chances of contact with LVS, facilitating the spread of the disease. The strong belief in these cultural practices and traditions hinders Lassa fever control measures in affected regions [89,119]. Furthermore, Nigeria's multilingual nature poses a barrier to the success of Lassa fever interventions by non-indigenous healthcare workers [89].

Illiteracy and poor public awareness and education: The level of awareness among Nigerian people about Lassa fever significantly impacts the success of combating the disease. Evidence shows that community knowledge of Lassa fever in Nigeria is very poor [96]. Poor community awareness and education are key risk factors for the spread of Lassa fever [66]. Media campaigns aimed at raising awareness have had limited impact in rural regions, resulting in insufficient knowledge about preventive measures and curative practices [120,121], emphasizing the need for improved health behavior modifications following health campaigns [120].

Illiteracy further exacerbates the poor reception of media coverage on Lassa fever, as educated individuals, who have better access to the internet and mass media, tend to have greater awareness [50]. Education has been shown to promote awareness and positive health-seeking behavior [16,105]. Specifically, Ilesanmi., *et al*. [16] found a statistically significant effect of education on knowledge of Lassa fever, with those having at least a secondary education demonstrating better knowledge compared to those with lower educational qualifications. Also a study by Gobir., *et al*. [122] found that good knowledge of Lassa fever was independently associated with maintaining good housing standards. This underscores the importance of education in enhancing awareness and understanding of key health

messages [16]. To address the knowledge gap, information should be disseminated through all available communication channels to reach households effectively [61].

Misdiagnosis and weak healthcare infrastructure: African healthcare systems' core challenges have been identified as inadequate human resources, insufficient healthcare systems, and poor leadership and management [123]. Every year, Nigeria, Africa's most populous country, faces numerous public health challenges that strain its inadequate health facilities and resources [124]. Lassa fever presents with nonspecific symptoms that often overlap with other endemic viral infections, frequently leading to misdiagnosis as malaria [125]. In endemic regions, individuals with these initial symptoms are typically tested for Lassa virus (LASV) only after empirical treatment with antimalarials and antibiotics fails [126]. Despite high awareness of Lassa fever among medical practitioners, there is limited access to affordable and simple tests for timely confirmation in the region [127]. This limitation can delay the time between suspecting and confirming cases, affecting disease outbreak and control efforts [128].

The recommended diagnostic tests, such as commercial PCR assays, require well-equipped, high-containment laboratories and trained staff to handle the highly infectious samples safely. Such infrastructure is often unavailable in primary or secondary health-care institutions where patients first seek care [126]. At present, health system capacity is weak as most Government owned health facilities in Nigeria lack facility for confirmatory diagnosis of Lassa fever [129]. Presently, only three functional laboratories equipped for LF samples analysis employing the use of polymerase chain reaction (PCR) are located in Lagos, Abuja and Irrua [130]. Additionally, the detection and confirmation of Lassa fever and other emerging viral diseases necessitate Biosafety Level 4 (BSL-4) facilities, which are scarce in Africa [131]. The extensive genetic variation of LASV can also lead to primer probe failures and false-negative results [125].

The weak healthcare delivery system in Nigeria, largely due to policymakers misplaced priorities in allocating sufficient resources to health institutions, continues to impede effective control of emerging and re-emerging infectious diseases, including Lassa fever [129]. Currently, LASV diagnosis relies on support from international donors. Delays in specimen transportation and poor quality of samples submitted to reference laboratories further hinder early diagnosis and favorable treatment outcomes. The Federal Government, through the Federal Ministry of Health (FMoH) and the Nigeria Centre for Disease Control (NCDC), needs to strengthen the healthcare delivery system to effectively contain Lassa fever and other emerging and re-emerging infectious diseases in Nigeria [129].

Shortage of medical practitioners: Nigeria's health system suffers from a shortage of healthcare personnel, who also face significant risks of infection due to inadequate facilities and protective measures [130,132]. Lassa fever, with its nonspecific symptoms, can infect health workers before a diagnosis is made, often due to the lack of personal protective equipment and other essential resources [133]. Pandemics and outbreaks negatively impact the work attitudes of frontline healthcare workers [134,135].

Over the years, the emigration of physicians from sub-Saharan Africa (SSA) and Nigeria in particular has continued to assume very disturbing trends [136]. In Nigeria, the internal and international migration of medical practitioners has significantly challenged public health systems, exacerbating already weakened healthcare systems and widening the global health inequalities gap [137]. Nigeria loses tens of millions of dollars annually by training medical doctors who subsequently leave the country [138]. Medical practitioners migrate from some African countries, particularly Nigeria, to high-income countries due to poor pay, irregular salary payments, poor working conditions (extra hours due to insufficient staff, lack of diagnostic facilities), and a lack of social amenities, making it difficult to maintain a good standard of living [139]. These factors contribute to Africa having the lowest density of medical professionals relative to the population worldwide [140].

Government negligence: Negligence by the Nigerian government towards healthcare has significantly contributed to the high mortality rates associated with Lassa fever observed annually [93]. Historically, government policies in Africa, including Nigeria, have paid inadequate attention to public health and welfare. This neglect is evident in the lack of substantial welfare packages, poor provision

of relief materials during disease outbreaks, inadequate research funding, and ineffective implementation of disease prevention and control programs [89]. The lack of political will to prioritize and address Lassa fever outbreaks has been a major challenge in preventing and controlling the disease. Since the first diagnosis of Lassa fever, the Nigerian government has provided only superficial support for managing and controlling the virus. Nigeria's health system remains weak and underfunded, with many intervention programs relying on foreign aid, often driven by research interests rather than local needs. Additionally, the government's failure to ensure proper waste management has exacerbated rodent populations, which are the primary reservoir for the Lassa virus. The increase in rodent populations directly correlates with higher incidence rates of Lassa fever [89].

Weak surveillance and lack of proper reporting: One of the factors militating against an effective national Lassa fever response includes weak surveillance reporting [129]. The World Health Organization (WHO) posits that Nigeria's capacity to fully implement disease surveillance and initiate appropriate public health measures has contributed to repeated Lassa fever outbreaks at both state and national levels [141]. Despite the lingering threats posed by LASV, there is a lack of comprehensive data and often conflicting reports of Lassa fever cases in Nigeria. With a population density of 248 people per square kilometer [142], disease surveillance and contact tracing can be challenging in densely populated areas, where the disease spreads faster among the population. If rodents are present, the number of cases may increase exponentially [129]. There is an urgent need to strengthen and reinforce active surveillance, contact tracing, and continuous outbreak investigation [129]. This can be achieved through training and providing logistical support to disease surveillance and notification officers involved in surveillance activities, facilitating prompt reporting of cases at ward, local government, and state levels [129].

Social unrest: 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. Most of the states hosting large numbers of internally displaced persons fleeing Boko Haram insurgents such as Borno, Abuja, Bauchi, Gombe, Kano, Plateau, Taraba and Edo states have recorded an outbreak of Lassa fever [143]. 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 [144].

Conclusion

The persistent recurrence of Lassa fever in Nigeria shows significant challenges in the country's public health response capabilities. Key drivers such as poverty, inadequate healthcare infrastructure, cultural practices, low public awareness, and government neglect have contributed to an enabling environment where the disease can proliferate. These challenges underscore the critical gaps in Nigeria's ability to prevent, and control Lassa fever outbreaks effectively. Improving outcomes will require a comprehensive approach that strengthens healthcare systems, enhances diagnostic and surveillance capacities, and engages communities through education and culturally sensitive interventions. Sustainable leadership commitment in the health sector is also vital for strengthening integrated outbreak surveillance and intervention. Addressing these systemic issues, is essential to mitigate the impact of Lassa fever and better protect public health in Nigeria.

Recommendations

Strengthening health services and advancing Nigeria's economic and sanitary conditions are essential to bringing Lassa fever under control. Sustained efforts will require guaranteed political commitment and a reevaluation of the government's role in the health sector to enhance effectiveness. Strong leadership at both regional and national levels is crucial, particularly from key entities like the Ministries of Health and the Nigeria Centre for Disease Control, to ensure coordinated and impactful action against the Lassa fever disease.

Collaborative multi-sectorial initiatives are needed to design a reservoir map tailored to proactive solutions against zoonotic disease threats in Nigeria. International cooperation for research should be reinforced to bridge knowledge gaps in areas such as diagnosis,

ecology and transmission of the virus, genetic diversity and lineage distribution, accurate mapping of at-risk areas, correlates of immune protection. This is to help to develop effective medical countermeasures that are tailored to specific population needs.

Finally, strengthening active and passive surveillance is crucial for a better understanding of the disease's epidemiology. As Lassa fever is a neglected tropical disease with limited funding, public health interventions must be guided by appropriate modeling to target at-risk populations effectively.

Availability of Data and Materials

All data supporting the findings of this study are included in the list of references and can be obtained at the Nigeria Centre for Disease Control (NCDC) http://www.ncdc.gov.ng/reports.

Conflict of Interest

There was no observed conflict of interest among authors to the best of our knowledge.

Funding Support

None.

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