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Lassa fever outbreak across two tertiary hospitals in Rivers State, Nigeria: clinical spectrum, healthcare-associated infection, contact investigation and public health response

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Lassa fever outbreak across two tertiary hospitals in Rivers State, Nigeria: clinical spectrum, healthcare-associated infection, contact investigation and public health response

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Abstract

Background

Lassa fever (LF) remains a major public health threat in Nigeria, with outcomes influenced by timely diagnosis and treatment and by potential healthcare-associated transmission. We characterised confirmed LF cases and conducted contact investigations at two tertiary hospitals in Rivers State, Nigeria, during the 2024 outbreak.

Methods

We conducted a descriptive two-centre case series of confirmed LF cases identified at the University of Port Harcourt Teaching Hospital (UPTH) and Rivers State University Teaching Hospital (RSUTH) from January 23 to August 13, 2024. Cases were confirmed by real-time reverse-transcription polymerase chain reaction (RT-PCR) for Lassa virus. Clinical, epidemiological, laboratory, treatment, and outcome data were obtained from hospital and public health records. Contact investigations included risk stratification, 21-day active surveillance, clinical assessment and RT-PCR testing of symptomatic contacts, and ribavirin post-exposure prophylaxis (PEP) for eligible high-risk contacts. Analysis was descriptive.

Results

Seven laboratory-confirmed cases were identified: five community-associated and two healthcare-associated infections among high-risk healthcare-worker contacts of the UPTH index case. Patients were aged 21–61 years, and four were male. Five patients had gastrointestinal and haemorrhagic manifestations (71.43%), while three had AKI and neurological manifestations (42.86%). Five patients survived, and two died, giving a case fatality proportion of 28.57%. Both deaths occurred in community-associated index cases before therapeutic ribavirin could be

administered. Contact surveillance detected the two healthcare-associated infections, which had mild clinical courses. At UPTH, 106 primary contacts were identified; 42 were high-risk, of whom 31 developed acute febrile illness, and two were confirmed with secondary LF. All 42 high-risk contacts received ribavirin PEP. At RSUTH, eight high-risk contacts were monitored; one received PEP, and none developed secondary infection. One survivor with severe renal disease required six haemodialysis sessions and was discharged after 18 days.

Conclusions

The LF outbreak demonstrated substantial clinical heterogeneity, ranging from mild healthcare-associated infection to severe multisystem disease and death. Contact investigation and prospective surveillance enabled detection of healthcare-associated secondary infections and facilitated targeted PEP. Strengthening early recognition, healthcare-worker protection, laboratory confirmation, contact surveillance, and timely treatment should remain priorities for LF preparedness and outbreak response in Nigeria.

Keywords: *Lassa fever; Nigeria; healthcare-associated infection; contact investigation; post-exposure prophylaxis; outbreak response; acute kidney injury; haemorrhagic fever*

Introduction

Lassa fever (LF) is an acute viral haemorrhagic disease caused by the Lassa virus (LASV) and is endemic in several West African countries, with Nigeria accounting for a substantial proportion of reported cases. In Nigeria, transmission occurs year-round with marked seasonal variation, and national surveillance has documented infection across multiple regions rather than within a small number of historically recognised foci [1,2]. This broad distribution means that LF may be encountered in tertiary hospitals that do not routinely manage large numbers of cases, underscoring the importance of diagnostic vigilance and preparedness beyond established treatment centres.

The clinical spectrum of LF is broad. Infection may be asymptomatic or present as a nonspecific febrile illness, whereas severe disease can lead to multisystem involvement, including haemorrhage, neurological dysfunction, hepatic injury, hypotension, and acute kidney injury (AKI) [3]. Prospective Nigerian data have identified AKI, physiological deterioration, elevated alanine aminotransferase (ALT), and higher viral burden as important predictors of mortality, and more recent evidence has further underscored the association between AKI and adverse outcomes [4,5]. The marked variation in clinical presentation and severity can therefore complicate recognition, particularly in the early phase of illness.

Early diagnosis remains challenging because the initial manifestations of LF overlap substantially with those of common causes of acute febrile illness (AFI) in Nigeria, particularly malaria and bacterial sepsis [3]. This diagnostic ambiguity has clinical consequences, as patients may receive treatment for more common conditions before LF is considered, allowing the disease to progress and increasing healthcare exposure before appropriate infection prevention and control (IPC) measures are instituted. Delayed presentation is also common; in a national

analysis of laboratory-confirmed cases, almost half of patients presented to healthcare facilities more than six days after symptom onset [6]. Recent prospective evidence showing frequent malaria coinfection among symptomatic patients with confirmed LF further indicates that malaria and LF may coexist rather than represent mutually exclusive diagnostic alternatives [7].

Delayed recognition is a major driver of healthcare-associated transmission. Transmission from infected patients to healthcare workers has been repeatedly documented during Nigerian outbreaks, particularly when diagnosis occurs after exposure-prone care has already taken place. During the 2018 national outbreak, healthcare workers accounted for a substantial proportion of confirmed infections, and an investigation of a tertiary-facility cluster identified delayed recognition and inadequate IPC practices as key contributors to occupational transmission [8]. These events show that the risk of LF extends beyond designated treatment centres to emergency departments, intensive care units (ICU), and other clinical settings where invasive procedures may be required before the diagnosis is established.

Once an index case is suspected or confirmed, effective control requires more than isolation and laboratory confirmation. Identifying and risk-stratifying contacts, active surveillance, prompt investigation of symptomatic contacts, occupational monitoring, and appropriate post-exposure management are key components of outbreak response [8,9]. Previous Nigerian investigations have shown that structured contact follow-up can identify exposed healthcare workers and facilitate early detection of secondary infection, while also highlighting the substantial operational workload generated by a single index case [9,10]. Importantly, febrile illness among contacts is not synonymous with LASV infection, so clearly distinguishing exposure, symptomatic illness, and laboratory-confirmed secondary infection is essential for interpreting outbreak investigations.

Despite the substantial Nigerian literature on LF, few reports have integrated the clinical spectrum of confirmed infection with healthcare-associated transmission, prospective contact investigation, active surveillance, and practical response within individual tertiary hospitals [8,9]. This integrated perspective is particularly relevant where LF may initially be obscured by common febrile diagnoses and where high-risk exposure can occur before infection is recognised. We therefore describe seven laboratory-confirmed LF cases identified across two tertiary hospitals in Rivers State, Nigeria, during the 2024 outbreak, focusing on clinical presentation and outcomes, healthcare-associated infections, contact investigation, active surveillance, post-exposure management, and outbreak-response activities. We further consider the implications of these findings for early clinical recognition, IPC, and preparedness for LF in tertiary healthcare settings.

2. Methods

2.1 Study design and setting

We conducted a two-centre descriptive case series with prospective contact investigation at the University of Port Harcourt Teaching Hospital (UPTH) and Rivers State University Teaching Hospital (RSUTH), two tertiary referral hospitals in Rivers State, southern Nigeria. Case ascertainment occurred from January 23 to August 13, 2024. Confirmed cases were followed beyond the case ascertainment period until discharge or death.

The study incorporated clinical characterisation of laboratory-confirmed LF cases, contact identification and risk stratification, prospective monitoring of contacts, laboratory testing of symptomatic contacts, post-exposure prophylaxis (PEP), and documentation of IPC and other outbreak-response activities.

2.2 Case identification and laboratory confirmation

Patients presenting with AFI and clinical or epidemiological features compatible with LF were evaluated according to the Nigerian national LF case-management guideline. Clinical suspicion was based on fever with compatible symptoms, relevant epidemiological exposure, lack of response to treatment for common causes of AFI, or clinical features suggestive of severe viral haemorrhagic disease. Patients requiring investigation were isolated and managed with appropriate IPC precautions while diagnostic specimens were obtained [11,12].

Blood samples from suspected cases were submitted to the National Reference Laboratory in Gaduwa, Abuja, for LASV testing using real-time reverse-transcription polymerase chain reaction (RT-PCR). A laboratory-confirmed case was defined as a suspected or clinically compatible case with a positive LASV RT-PCR result.

2.3 Clinical data collection

Clinical and epidemiological data were extracted from hospital, laboratory, infection-control, and public health records using a structured data collection approach. Variables included age, sex, occupation, healthcare facility, epidemiological classification, relevant exposure history, duration of illness before presentation, presenting symptoms and signs, major laboratory abnormalities, complications, antiviral therapy, supportive management, intensive care requirements, renal replacement therapy (RRT), length of hospital stay, and clinical outcome.

Cases were classified as community-associated when no healthcare-associated exposure to a confirmed LF case was identified. Cases were classified as healthcare-associated when infection occurred after documented occupational exposure while caring for a confirmed case, and no alternative epidemiological exposure was identified.

2.4 Assessment of disease severity and complications

Disease severity was assessed descriptively based on clinical presentation, organ dysfunction, complications, and the intensity of supportive care required during hospitalisation. Major severe manifestations observed among confirmed cases were documented, including AKI, severe neurological manifestations such as seizures, confusion or coma, significant bleeding, respiratory compromise, severe anaemia requiring transfusion, sepsis or hypovolaemic shock, and other clinically important organ dysfunction [11].

Major complications and clinically relevant abnormalities were recorded, including AKI, neurological manifestations, haemorrhage, hepatic dysfunction, thrombocytopenia, cardiovascular abnormalities, respiratory compromise, and other documented complications. The study also recorded requirements for intensive care, RRT, blood transfusion, and other major supportive interventions.

2.5 Contact identification and risk categorisation

After identifying confirmed cases, the hospital outbreak-response teams, in collaboration with relevant public-health personnel, conducted contact investigations. Contacts were identified through patient and family interviews, review of clinical records, healthcare-worker rosters, exposure histories, and other available epidemiological information.

Each identified contact was assessed based on the nature, intensity, and circumstances of exposure and categorised as no-risk, low-risk, or high-risk in accordance with national LF guidance [11]. High-risk exposures included unprotected contact with blood or other body fluids; exposure to mucous membranes or broken skin; sharps injuries; unprotected handling of clinical

specimens; and healthcare workers exposed during exposure-prone procedures without appropriate personal protective equipment (PPE).

2.6 Contact monitoring and active surveillance

Identified contacts were monitored for 21 days following their last possible exposure, consistent with the national LF case management guideline [11]. Contacts received information about LF symptoms and instructions to report fever or other compatible symptoms promptly.

During monitoring, development of fever or other compatible symptoms prompted clinical assessment and laboratory investigation. AFI occurring during contact monitoring was documented regardless of the eventual diagnosis. Empirical treatment for other causes of febrile illness, including presumed malaria, was recorded as part of clinical management and was not considered evidence of malaria unless supported by appropriate diagnostic testing.

2.7 Laboratory investigation of contacts

Contacts who developed fever or other symptoms compatible with LF during the monitoring period underwent clinical assessment and LASV testing by real-time RT-PCR through the established diagnostic pathway. Secondary laboratory-confirmed LF was defined as a positive LASV RT-PCR result in a contact identified during the investigation of a confirmed case.

Negative RT-PCR results among symptomatic contacts were recorded during the contact investigation and were not classified as LF.

2.8 Post-exposure prophylaxis

Ribavirin PEP was offered to eligible high-risk contacts in accordance with national guidelines. Oral ribavirin was administered at 500 mg every 6 hours for 7 days [11].

Contacts receiving PEP remained under the 21-day post-exposure monitoring system. PEP administration, adherence, and documented adverse effects were obtained from clinical and contact-monitoring records.

2.9 Infection prevention and control and outbreak response

Outbreak-response activities were documented in clinical, infection-control, and public-health records. These included notifying suspected and confirmed cases, isolating patients, implementing or reinforcing IPC measures, identifying contacts and assessing risk, conducting active surveillance, laboratory investigation, monitoring healthcare workers, using PPE, and communicating risks or raising staff awareness [11,12].

For healthcare-associated exposures, the clinical and occupational circumstances of exposure were reviewed, including procedures that may involve contact with blood, body fluids, or other potentially infectious materials.

2.10 Outcomes

The principal descriptive outcomes were the clinical spectrum of laboratory-confirmed LF, major complications, treatment requirements, and clinical outcomes, including recovery or death. Additional outcomes included healthcare-associated infection among exposed healthcare workers, contact-risk categories, AFI during contact monitoring, laboratory-confirmed secondary LF among contacts, use of ribavirin PEP, documented PEP-related adverse effects, and implementation of major outbreak-response measures.

2.11 Data analysis

Data were analysed using descriptive statistics. Categorical variables were summarised using frequencies and percentages. Continuous variables were summarised using means and standard deviations or medians and ranges, depending on data distribution and completeness. Percentages were calculated using the available denominator for each variable. No inferential statistical modeling was performed because of the small number of confirmed cases and the study's descriptive nature.

3. Results

3.1 Epidemiological and clinical characteristics of confirmed cases

Seven laboratory-confirmed LF cases were identified between January 23 and August 13, 2024: six at UPTH and one at RSUTH. Patients were 21–61 years old; four were male and three were female. Five cases were community-associated, and two were healthcare-associated infections identified among high-risk healthcare-worker contacts of the UPTH index case. Table 1 presents individual demographic, epidemiological, and presenting clinical characteristics.

Table 1. Demographic, epidemiological, and clinical characteristics of seven laboratory-confirmed Lassa fever cases in Rivers State, Nigeria, January–August 2024

Case	Facility	Epidemiological classification	Age, years	Sex	Occupation	Date of presentation	Principal clinical presentation	Outcome
1	UPTH	Community-associated index case	21	Female	Undergraduate	23 Jan 2024	High-grade febrile illness with altered consciousness, seizures, hydrocephalus, and other neurological manifestations	Died

2	UPTH	Community-associated	24	Male	Undergraduate	29 Jan 2024	Prolonged fever with abdominal symptoms, vomiting, diarrhoea, haematemesis and haematochezia	Survived
3	UPTH	Healthcare-associated; high-risk contact of Case 1	34	Female	ICU nurse	During 21-day post-exposure monitoring	Mild acute febrile illness with fever, headache, sore throat, and cough	Survived
4	UPTH	Healthcare-associated; high-risk contact of Case 1	40	Female	ICU physician	During 21-day post-exposure monitoring	Mild AKI with fever, headache, malaise and anorexia	Survived
5	RSUTH	Community-associated index case	61	Male	Trader	20 Feb 2024	High-grade fever with gastrointestinal symptoms, subsequent bleeding, oliguria, and respiratory compromise	Died
6	UPTH	Community-associated	44	Male	Driver	28 Feb 2024	Febrile illness with vomiting, persistent fever, gross haematuria and hepatic enzyme elevation	Survived
7	UPTH	Community-associated	56	Male	Trader	13 Aug 2024	Persistent fever with haematuria, severe AKI and uraemic encephalopathy	Survived

The cases comprised two hospital investigations: the UPTH investigation, which identified two healthcare-associated infections among exposed healthcare workers, and the RSUTH investigation, which detected no secondary infections among monitored high-risk contacts.

3.2 Clinical spectrum and major complications

The clinical spectrum ranged from mild AKI in healthcare-associated cases to severe multisystem disease. Gastrointestinal and haemorrhagic manifestations were each documented in

five patients (71.43%), while AKI and neurological manifestations each occurred in three (42.86%).

The most extensive neurological involvement occurred in the UPTH index case, who developed altered consciousness, seizures, hydrocephalus, and cerebral infarction. The RSUTH index case developed progressive systemic deterioration with bleeding, oliguria, and respiratory compromise. Among survivors, Case 7 developed severe AKI with uraemic encephalopathy requiring RRT, while Case 6 had marked elevation of hepatic enzymes that improved during treatment. Other laboratory abnormalities included thrombocytopenia, anaemia, and biochemical evidence of hepatic and renal dysfunction. Table 2 presents early laboratory findings among seven laboratory-confirmed LF cases.

Table 2. Initial and early laboratory investigations among seven laboratory-confi med Lassa fever cases in Rivers State, Nigeria

Case	**Haemoglobin, g/dL**	**WBC, ×10⁹/L**	**Platelets, ×10⁹/L**	**Creatinine, mg/dL**	**Urea, mmol/L**	**Principal hepatic abnormalities**	**Other relevant findings**
1	14.70	16.70	281	1.18	5.00	—	Progressive renal dysfunction; subsequent AKI
2	12.00	13.00	180	0.75	5.50	AST 98 U/L; ALT 65 U/L; ALP 325 U/L	Bilirubin 27 µmol/L; *P. falciparum* detected
3	14.00	6.00	234	0.90	7.00	AST 30 U/L; ALT 20 U/L	No major baseline biochemical abnormality
4	11.00	8.00	190	0.75	6.40	AST 20 U/L; ALT 15 U/L	No major baseline biochemical abnormality

5	12.20	3.60	102	1.08	4.60	AST 402 U/L; ALT 1,747 U/L; ALP 731 U/L; GGT 1,695 U/L	Bilirubin 60 µmol/L; marked thrombocytopenia
6	11.00	15.00	145	1.02	5.60	AST 215 U/L; ALT 147 U/L; ALP 236 U/L; GGT 195 U/L	Bilirubin 42 µmol/L; gross haematuria; *P. falciparum* detected
7	15.00*	7.80*	181*	0.86*	4.20*	AST 20 U/L; ALT 15 U/L*	Subsequent progressive azotaemia; later creatinine 5.75 mg/dL and severe electrolyte abnormalities

**Initial values from the referring facility; subsequent values during UPTH admission demonstrated progressive renal dysfunction and haematological changes.*

Abbreviations: AKI, acute kidney injury; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyl transferase; UPTH, University of Port Harcourt Teaching Hospital; WBC, white blood cell count.

3.3 Treatment and clinical outcomes

Five patients survived, and two died, giving an overall case fatality proportion of 28.57%. Both deaths occurred in community-associated index cases with rapidly progressive multisystem disease. Neither received therapeutic ribavirin before death. The UPTH index case died before LF-specific treatment could be initiated, while the RSUTH index case died on the third day of admission before the positive RT-PCR result was available.

All five survivors received ribavirin at some point during their clinical course. In Case 2, ribavirin was initiated after RT-PCR confirmation, by which time the patient had already made substantial clinical recovery. Cases 6 and 7 received intravenous therapeutic ribavirin, whereas Cases 3 and 4 received oral ribavirin as PEP.

Case 7 required the most intensive supportive care, including six haemodialysis sessions, and was discharged after 18 days of hospitalisation. All five survivors recovered, with no documented deaths during follow-up. Table 3 details treatment, supportive interventions, and outcomes.

Table 3. Disease progression, major complications, organ support and treatment outcomes among seven laboratory-confirmed Lassa fever cases

Case	**Major complications/organ involvement**	**Organ support or major interventions**	**Ribavirin**	**Hospital course/outcome**
1	Severe neurological disease, hydrocephalus, cerebral infarction, bleeding and AKI	Ventriculostomy/EVD, intubation and ICU care	Not administered before death	Rapid deterioration; died before LF-specific treatment
2	Gastrointestinal and haemorrhagic manifestations; no documented AKI	Supportive care and antimicrobial treatment for initial differential diagnoses	Oral, after discharge	Clinical recovery; discharged 9 Feb 2024
3	Mild febrile illness; no documented AKI, major neurological or haemorrhagic complications	Home isolation and clinical monitoring	Oral PEP ×10 days	Recovered; remained clinically well on follow-up
4	Mild febrile illness; no documented AKI, major neurological or haemorrhagic complications	Home isolation and clinical monitoring	Oral PEP ×10 days	Recovered; remained clinically well on follow-up
5	Bleeding, severe hepatic dysfunction, oliguria and respiratory compromise	Supportive care; progressive deterioration	Not administered before death	Died on day 3 of admission, before positive RT-PCR result became available
6	Gross haematuria and marked hepatic enzyme elevation	Supportive care and antimicrobial treatment;	IV therapeutic ribavirin ×10 days	Fever and haematuria resolved; discharged after recovery

		no renal replacement therapy		
7	Severe AKI, uraemic encephalopathy, haematuria, anaemia and biochemical abnormalities	Six haemodialysis sessions, oxygen, blood transfusion and supportive treatment	IV therapeutic ribavirin ×10 days	Progressive improvement; discharged 31 Aug 2024 after 18 days

Abbreviations: *AKI, acute kidney injury; EVD, external ventricular drain; ICU, intensive care unit; IV, intravenous; LF, Lassa fever; PEP, post-exposure prophylaxis; RT-PCR, reverse-transcription polymerase chain reaction.*

3.4 Healthcare-associated infections

Two healthcare-associated infections occurred among healthcare workers exposed while managing the UPTH index case, including during airway management performed without adequate protection. Both developed febrile illness during post-exposure monitoring and later tested positive for LASV by RT-PCR.

Their illness was clinically less severe than that of the index case. Neither developed documented AKI, major neurological complications, or haemorrhagic manifestations, and both recovered after oral ribavirin PEP.

3.5 Contact investigation and active surveillance

At UPTH, 106 primary contacts were identified: 42 high-risk (39.62%), 60 low-risk (56.60%), and 4 no-risk (3.77%). Of the high-risk contacts, 31 (73.81%) developed AFI during monitoring. Of these, 29 (93.55%) received empirical treatment for presumed uncomplicated Plasmodium falciparum malaria, while two (6.45%) were confirmed to have LF by RT-PCR; both were healthcare workers.

At RSUTH, staff monitored eight high-risk contacts, and none developed laboratory-confirmed LF. The total number of primary contacts at RSUTH was unavailable, so the proportion classified as high-risk could not be calculated. Table 4 summarises contact investigation findings.

Table 4. Contact investigation, active surveillance and post-exposure prophylaxis following laboratory-confirmed Lassa fever cases at two tertiary hospitals in Rivers State, Nigeria

Facility	Contact group	Number	Acute febrile illness	RT-PCR-confirmed LF	Ribavirin PEP	Documented PEP adverse effects
UPTH	All primary contacts	106	—	—	—	—
UPTH	High-risk	42 (39.62%)	31 (73.81%)	2/31 (6.45% of febrile high-risk contacts)	42/42 (100%)	Dizziness and weakness documented
UPTH	Low-risk	60 (56.60%)	—	0/8	Not routinely indicated	—
UPTH	No-risk	4 (3.77%)	—	0	Not indicated	—
RSUTH	High-risk contacts	8	No secondary LF documented	0	1/8 (12.50%)	Weakness documented

3.6 Implementation of post-exposure prophylaxis

All 42 high-risk UPTH contacts received oral ribavirin PEP. At RSUTH, one of the eight high-risk contacts received prophylaxis. Dizziness and weakness were documented among UPTH contacts receiving prophylaxis, and the single RSUTH contact who received prophylaxis reported weakness.

3.7 Outbreak response

The response included case notification and isolation, IPC reinforcement, contact identification and risk assessment, active surveillance, laboratory testing of symptomatic contacts, healthcare-worker monitoring, PEP, and coordination with public health authorities.

At UPTH, the hospital LF outbreak committee coordinated the response, including hospital-wide awareness and training on LF and IPC for viral haemorrhagic fever. Figure 1 shows the temporal relationship between case recognition and major response milestones across the two investigations.

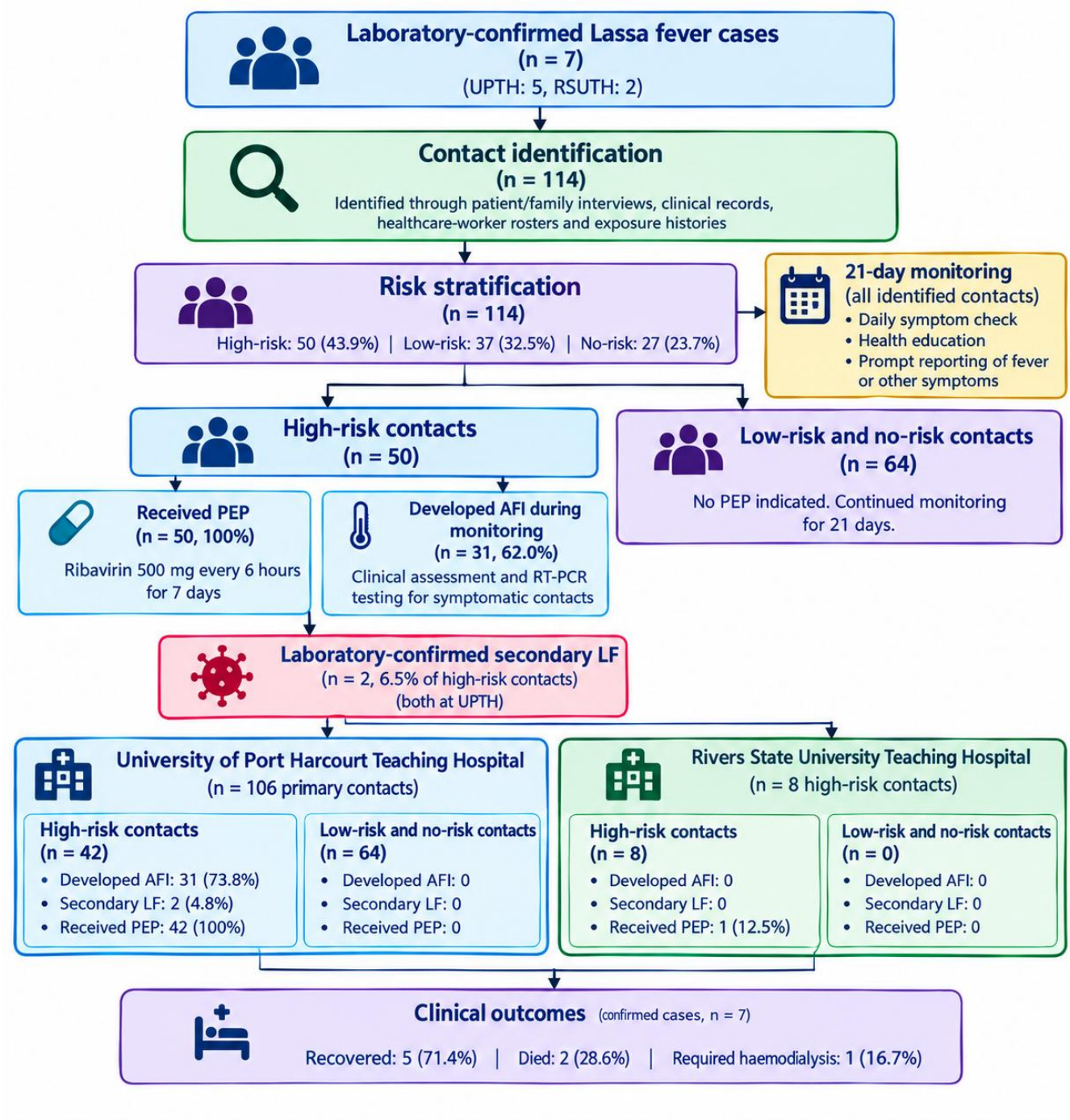


Figure 1. Temporal sequence of the seven confirmed Lassa fever cases and major outbreak-response milestones, Rivers State, Nigeria, 2024

4. Discussion

This two-centre case series of seven laboratory-confirmed LF cases managed at two tertiary hospitals in Rivers State during the 2024 outbreak highlights three closely interconnected features of LF in routine practice: substantial clinical heterogeneity, the potential for healthcare-associated transmission when infection is not recognised before high-risk procedures, and the operational importance of systematic contact investigation and active surveillance. The cases ranged from acute undifferentiated febrile illness to severe multisystem disease involving the central nervous system (CNS), kidneys, liver, and haemostatic system. Five patients survived, and two died, while two healthcare-associated secondary infections were identified during surveillance of high-risk contacts of the UPTH index case.

Clinical heterogeneity and severe disease

The clinical spectrum observed in this study mirrors the broad phenotype described in contemporary LF cohorts, where fever and constitutional symptoms may be accompanied by gastrointestinal, neurological, renal, hepatic, and haemorrhagic manifestations [3]. Importantly, disease severity varied substantially among patients. The two healthcare-associated infections remained clinically mild, whereas several community-associated patients developed extensive organ dysfunction. This heterogeneity matters clinically because the absence of a classical haemorrhagic presentation does not reliably indicate a benign course.

AKI and neurological manifestations occurred in three patients, including both hospital index cases and Case 7. Prospective Nigerian data from Irrua, Edo State, identified kidney injury, physiological deterioration, elevated ALT, and higher viral burden as predictors of mortality, while more recent Nigerian data from Owo, Ondo State, similarly associated AKI, oliguria, and

haematuria with adverse outcomes [4,13]. Case 7 demonstrated the potential for rapid renal deterioration: creatinine rose from 86 to 575 μmol/L, accompanied by progressive oliguria, hyperkalaemia, and uraemic manifestations, ultimately requiring six haemodialysis sessions. This course supports serial monitoring of renal function, urine output, and electrolytes rather than reliance on a single early biochemical assessment.

Case 1 presented a distinct form of severe disease dominated by neurological manifestations, including altered consciousness, seizures, obstructive hydrocephalus, and cerebral infarction. Although neurological involvement is recognised in LF, its pathogenesis remains incompletely defined [14]. The markedly elevated cerebrospinal fluid (CSF) protein concentration in this patient, without significant pleocytosis, should be interpreted cautiously. In the context of obstructive hydrocephalus and ventricular instrumentation, this finding may have reflected impaired CSF circulation, blood contamination, or procedural effects. Nevertheless, the case emphasizes that LF may initially present as a neurological syndrome, prompting consideration of alternative diagnoses.

Haemorrhagic manifestations were documented in five patients and ranged from haematemesis and haematochezia to haematuria, cannula-site bleeding, and bleeding through an external ventricular drain. These findings should therefore be interpreted within the clinical context rather than assumed to represent a uniform haemorrhagic phenotype. Overall, the observations support the view of LF as a potentially progressive multisystem infection in which the pattern of organ dysfunction may be more informative than bleeding alone [5].

Diagnostic overlap with malaria and bacterial sepsis

A major practical challenge the study highlighted was distinguishing LF from common causes of AFI. Several patients were initially treated for malaria, bacterial sepsis, or both before persistent symptoms or new manifestations, such as haematuria, bleeding, neurological deterioration, or organ dysfunction, prompted consideration of LF. This overlap is particularly important in malaria-endemic settings, where a positive malaria diagnosis does not necessarily exclude LF. Recent prospective data from the ENABLE 1.0 study found malaria coinfection in 27 (69%) of 39 symptomatic RT-PCR-confirmed LF cases, supporting the possibility that malaria and LF may coexist and that malaria positivity should not necessarily exclude LF [15].

The UPTH contact investigation underscores this diagnostic complexity. Of 42 high-risk contacts, 31 developed AFI during surveillance; 29 were empirically treated for presumed uncomplicated *Plasmodium falciparum* malaria, and RT-PCR confirmed LF in two. The 29 contacts should not be considered confirmed malaria cases because the available data do not establish malaria as the definitive cause of their illness. More importantly, the findings show that fever among exposed contacts should trigger diagnostic reassessment rather than serve as a diagnostic endpoint. In an exposed individual, treatment for a common febrile illness may need to proceed alongside investigation for LF when the clinical course remains atypical.

Limitations in rapid testing compound the diagnostic conundrum. Recent evaluations of the ReLASV Pan-Lassa antigen test using Nigerian samples have shown variable and insufficient sensitivity to reliably exclude infection [16]. Consequently, RT-PCR remains central to confirmation, and delays in obtaining definitive laboratory results can prolong the period during which clinical and infection-control decisions must be made under uncertainty.

Healthcare-associated transmission and contact investigation

The two healthcare-associated infections are among the most important findings of this study. Both occurred among high-risk contacts involved in managing the UPTH index case, including those performing airway management procedures without adequate protection. Both developed febrile illness during the 21-day monitoring period, and RT-PCR confirmed the illness, which remained mild throughout the clinical course.

Healthcare-associated transmission is a recurring feature of LF outbreaks in Nigeria. An investigation of a major tertiary-facility cluster during the 2018 outbreak identified delayed recognition and inadequate infection-prevention practices as key contributors to transmission and documented substantial infection among healthcare workers [8]. Studies of Nigerian Lassa treatment centres have likewise identified gaps in PPE use, staff training, and occupational exposure procedures [17,18]. The present findings therefore reinforce a recognisable transmission pathway: an unrecognised infectious patient receives exposure-prone care, healthcare workers become high-risk contacts, and the health system must then mobilise contact investigation, laboratory testing, and occupational surveillance.

The UPTH investigation also underscores the scale of the operational response that can arise from a single index case. Of 106 primary contacts identified, 42 were classified as high risk, 60 as low risk, and four as having no identified risk. Thirty-one high-risk contacts developed AFI, but only two were confirmed to have secondary LF. This distinction matters because febrile illness among contacts is a surveillance trigger, not evidence of transmission. Active surveillance identified the two secondary infections, showing that systematic monitoring can serve as an early case-finding mechanism rather than merely documenting exposure.

Comparable Nigerian investigations have shown that contact networks can be large and that secondary transmission does not necessarily occur even after substantial exposure [9,10]. The

present findings add an important contrasting observation: when high-risk healthcare exposures occur before diagnosis, the surveillance network may detect secondary infection despite subsequent monitoring and prophylaxis. The data consequently support prompt exposure-risk assessment and systematic occupational surveillance once LF is suspected.

Post-exposure prophylaxis and ribavirin

All 42 high-risk UPTH contacts received oral ribavirin PEP, whereas only one of eight documented high-risk contacts at RSUTH received prophylaxis. These figures describe outbreak-response practice but do not allow a comparative assessment of prophylactic effectiveness, particularly because the overall RSUTH contact denominator was unavailable and individual exposure and prophylaxis timing were incompletely documented.

The occurrence of confirmed LF in two healthcare workers receiving prophylaxis should therefore not be interpreted as prophylaxis failure. The study lacks sufficient information on exposure intensity, timing of prophylaxis initiation, adherence, and other determinants of infection. More broadly, uncertainty surrounding ribavirin extends to its therapeutic use. Although historical observational evidence suggested benefit when ribavirin was initiated early [19], subsequent systematic reviews have highlighted important methodological limitations in the evidence base [20,21].

The treatment experience here is similarly heterogeneous. Ribavirin exposure was documented in all five survivors, but one received oral therapy after substantial clinical recovery, two received PEP, and two received therapeutic intravenous ribavirin. Consequently, ribavirin cannot be attributed to either survival or clinical improvement. The recent Nigerian phase II trial

comparing favipiravir and ribavirin in mild LF signals a shift toward prospective evaluation of alternative therapeutics, but it has not yet resolved the efficacy of either agent [22].

Clinical recognition and implications for tertiary hospitals

The temporal sequence of cases shows that the LF response extends beyond individual patient diagnosis. The UPTH index case prompted a large contact investigation and revealed two healthcare-associated infections; a separate RSUTH index case prompted another contact investigation; and clinical assessment and laboratory testing identified subsequent community-associated cases. Across these events, the working diagnosis often changed as the illness evolved.

This supports dynamic diagnostic reassessment of patients with persistent or unexplained fever, particularly when new haematuria, bleeding, neurological manifestations, or progressive organ dysfunction emerge. In tertiary hospitals, preparedness should therefore extend beyond designated infectious-disease units to emergency departments, ICUs, procedure areas, and laboratories, where exposure may occur before LF is suspected. Airway management and other exposure-prone procedures warrant particular attention because they can expose multiple healthcare workers simultaneously.

The findings also underscore the importance of linking clinical care, laboratory diagnosis, and public health response. Case identification and management alone do not contain an outbreak; an effective response depends on rapid recognition, appropriate precautions, exposure-risk classification, active contact monitoring, and access to confirmatory testing. Case 5, in whom RT-PCR confirmation became available after death, further emphasizes the importance of maintaining diagnostic and surveillance pathways even when disease progression is rapid.

Similarly, Case 7 demonstrates that survival from severe disease may depend not only on antiviral therapeutics but also on access to RRT, intensive monitoring, and supportive care.

Strengths and limitations

A principal strength of this study is the integration of laboratory-confirmed clinical data with contact investigation, active surveillance, post-exposure prophylaxis, and outbreak-response documentation across two tertiary hospitals in a historically low-burden state. This integration enabled the study to capture both the clinical spectrum of confirmed disease and healthcare-associated transmission stemming from an index case. The explicit distinction among high-risk exposure, AFI, and RT-PCR-confirmed secondary infection further strengthens the epidemiological interpretation.

The study has several limitations. The sample size was small, and the analysis was descriptive, precluding statistical inference and estimation of predictors of severity, mortality, or transmission. The tertiary-hospital setting may preferentially capture patients with more severe disease or diagnostic uncertainty and may not represent the full community spectrum. Clinical and laboratory documentation was not uniform across all patients, limiting some longitudinal comparisons. Detailed information on exposure timing, adherence, and the precise timing of PEP was insufficient to assess its effectiveness. The total primary-contact denominator at RSUTH was unavailable, preventing calculation of the proportion of all contacts classified as high risk and limiting comparison between the two investigations. Genomic sequencing was not performed, so the suspected epidemiological linkage between the two healthcare-associated infections and the UPTH index case could not be independently corroborated. Finally, ribavirin was administered in different therapeutic and prophylactic contexts without a control group;

therefore, neither survival nor clinical improvement can be causally attributed to antiviral treatment.

Conclusion

This study demonstrates the broad clinical spectrum of LF in two tertiary hospitals in Rivers State during the 2024 outbreak, ranging from mild AFI to severe multisystem disease with neurological, renal, haemorrhagic, and hepatic involvement. It also documents healthcare-associated transmission linked to high-risk exposure during the management of an unrecognised index case, with both secondary infections detected through active surveillance. The findings underscore the importance of maintaining diagnostic suspicion when common explanations, such as malaria or bacterial sepsis, do not fully account for the clinical course, particularly in patients with progressive organ dysfunction or relevant exposure histories.

At the health-system level, the findings reinforce the value of early infection-control activation, structured exposure-risk assessment, comprehensive contact surveillance, reliable molecular diagnosis, and access to organ-supportive care. The experience also highlights persistent evidence gaps surrounding post-exposure prophylaxis and therapeutic ribavirin. Strengthening the interface among clinical care, laboratory diagnosis, occupational surveillance, and public-health response may therefore offer a practical route to reducing both preventable healthcare-associated transmission and severe LF outcomes.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. The Research and Ethics Committees of UPTH and RSUTH approved the study. The study used routinely collected

clinical, laboratory, and public-health data, together with information generated during outbreak contact investigations. All data were de-identified before analysis and reporting. Individual-level information obtained during clinical care and contact investigations was handled confidentially and was accessible only to authorised members of the study and outbreak-response teams. Individual informed consent was not required for the use of routinely collected, de-identified data, in accordance with the determinations of the relevant research ethics committees.

Consent for publication

Not applicable because the manuscript uses routinely collected and de-identified data and does not include identifiable patient information or images.

Competing interests

The authors declare no competing interests.

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Authors' contributions

CO conceived the study and study design and drafted the manuscript. VG, HA, CN, and OM contributed to the contact investigation and data collection. CO, CN, and VG contributed to case management and laboratory interpretation. All authors critically reviewed the manuscript, approved the final version, and agreed to be accountable for all aspects of the work.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available because they contain potentially identifiable clinical and contact-investigation information. De-

identified data may be available from the corresponding author on reasonable request, subject to approval by the relevant institutional and/or public-health authorities and applicable ethical and data-protection requirements.

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Abbreviations

AFI — acute febrile illness

AKI — acute kidney injury

ICU – intensive care unit

IPC — infection prevention and control

LASV — Lassa virus

LF — Lassa fever

PEP — post-exposure prophylaxis

PPE — personal protective equipment

RRT — renal replacement therapy

RSUTH — Rivers State University Teaching Hospital

RT-PCR — reverse-transcription polymerase chain reaction

UPTH — University of Port Harcourt Teaching Hospital

References

1. Ilori EA, Frank C, Dan-Nwafor CC, Ipadeola OB, Krings A, Ukponu W, et al. Increase in Lassa fever cases in Nigeria, January–March 2018. *Emerg Infect Dis.* 2019;25(5):1026-1027.

2. Ipadeola O, Furuse Y, Ilori EA, Dan-Nwafor CC, Akabike KO, Ahumibe A, et al. Epidemiology and case-control study of Lassa fever outbreak in Nigeria from 2018 to 2019. *J Infect.* 2020;80(5):578-606.

3. Merson L, Bourner J, Jalloh S, Erber A, Salam AP, Flahault A, et al. Clinical characterization of Lassa fever: a systematic review of clinical reports and research to inform clinical trial design. *PLoS Negl Trop Dis.* 2021;15(9):e0009788.

4. Duvignaud A, Jaspard M, Etafo IC, Gabillard D, Serra B, Abejegah C, et al. Lassa fever outcomes and prognostic factors in Nigeria (LASCOPE): a prospective cohort study. *Lancet Glob Health.* 2021;9(4):e469-e478.

5. Okwuraiwe AP, Onyeaghala CA, Ozoude OT, Suleiman MO, Abdu-Aguye SN, Ezekwelu NJ, et al. Clinical outcomes of severe Lassa fever in West Africa: a systematic review and meta-analysis. *Int J Environ Res Public Health.* 2025;22(10):1504.

6. Chandra NL, Bolt H, Dan-Nwafor C, Ipadeola O, Ilori E, Namara G, et al. Factors associated with delayed presentation to healthcare facilities for Lassa fever cases, Nigeria 2019: a retrospective cohort study. *BMC Infect Dis.* 2021;21(1):143.

7. Enable Lassa Research Programme (Enable 1.0) Consortium. Incidence of symptomatic Lassa virus infection in West African countries (Enable 1.0 Lassa Research Study): a prospective, multisite, cohort study. *Lancet Glob Health.* 2026;14(7):103945.

8. Dan-Nwafor CC, Ipadeola O, Smout E, Ilori E, Adeyemo A, Umeokonkwo C, et al. A cluster of nosocomial Lassa fever cases in a tertiary health facility in Nigeria: description and lessons learned, 2018. *Int J Infect Dis.* 2019;83:88-94.

9. Iroezindu MO, Unigwe US, Okwara CC, Ozoh GA, Ndu AC, Ohanu ME, et al. Lessons learnt from the management of a case of Lassa fever and follow-up of nosocomial primary contacts in Nigeria during Ebola virus disease outbreak in West Africa. *Trop Med Int Health.* 2015;20(11):1424-1430.

10. Isa SE, Okwute A, Iraoyah KO, Nathan SY, Simji GS, Okolo MO, et al. Postexposure prophylaxis for Lassa fever: Experience from a recent outbreak in Nigeria. Niger Med J. 2016 Jul-Aug;57(4):246-50

11. Nigeria Centre for Disease Control. National guidelines for Lassa fever case management. Abuja: Nigeria Centre for Disease Control; 2018. Available from https://ncdc.gov.ng/themes/common/docs/protocols/92_1547068532.pdf (accessed on 7 September 2026)

12. Nigeria Centre for Disease Control. National guidelines on infection prevention and control for viral haemorrhagic fevers. Abuja: Nigeria Centre for Disease Control; 2019. Available from https://ncdc.gov.ng/themes/common/docs/protocols/111_1579986179.pdf (accessed on 7 September 2026)

13. Ojo LE, Hassan MO, Ojo OA, Subulade AA, Ihinmikaye I, Oyegunle OO, et al. Predictors of acute kidney injury and in-hospital mortality in patients with RT-PCR confirmed Lassa fever in Southwest Nigeria. Open Forum Infect Dis. 2026;13(7):ofag412.

14. Müller HCS, Erameh CO, Okoeguale J, Ileli SO, Onyeke IF, Adetunji AE, et al. Presence of Lassa virus RNA in cerebrospinal fluid indicating neuroinvasive Lassa fever in pediatric patients from Edo State, Nigeria. J Infect Dis. 2026;233(3):e611-e620.
15. Issifou AMD, Deha ARE, Yadouleton A, Yanclo AI, Adegnika AA, Tchibozo C, et al. Incidence of symptomatic Lassa virus infection in West African countries (Enable 1.0 Lassa Research Study): a prospective, multisite, cohort study. Lancet Glob Health. 2026;14(7):103945.
16. Chi HF, Etafo J, Fonkeng F, Olufunke GA, Ireneh R, Abejegah C, et al. Evaluation of the diagnostic accuracy of the ReLASV Pan-Lassa Antigen Rapid Test for Lassa Fever in Nigeria. PLOS Glob Public Health. 2025;5(4):e0004405.
17. Obionu IM, Ochu CL, Ukponu W, Okwor T, Dan-Nwafor C, Ilori E, et al. Evaluation of infection prevention and control practices in Lassa fever treatment centers in north-central Nigeria during an ongoing Lassa fever outbreak. J Infect Prev. 2021;22(6):275-282.
18. Holt A, Hornsey E, Seale AC, Rohan H, Bausch DG, Ihekweazu C, et al. A mixed-methods analysis of personal protective equipment used in Lassa fever treatment centres in Nigeria. *Infect Prev Pract.* 2021;3(3):100168
19. McCormick JB, King IJ, Webb PA, Scribner CL, Craven RB, Johnson KM, et al. Lassa fever. Effective therapy with ribavirin. N Engl J Med. 1986;314(1):20-26.
20. Cheng HY, French CE, Salam AP, Dawson S, McAleenan A, McGuinness LA, et al. Lack of evidence for ribavirin treatment of Lassa fever in systematic review of published and unpublished studies. Emerg Infect Dis. 2022;28(8):1603-1609.

21. Salam AP, Duvignaud A, Jaspard M, Malvy D, Carroll M, Tarning J, et al. Ribavirin for treating Lassa fever: a systematic review of pre-clinical studies and implications for human dosing. PLoS Negl Trop Dis. 2022;16(3):e0010289.
22. Erameh C, Okwaraeke K, Kleist C, Edeawe O, Adedosu N, Ekata E, et al. Favipiravir for Lassa fever: an open-label, randomized controlled phase 2 trial. Nat Med. 2026;32:2522-2532.