

Case Report

Severe Lassa Fever with Heart Failure and Respiratory distress in a Toddler: Survival Without Ribavirin Through Intensive Supportive Care

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ABSTRACT

Lassa fever (LF) remains a significant public health threat in West Africa, with Nigeria experiencing a case fatality rate (CFR) of 25.2% among confirmed cases in 2026. Intravenous ribavirin has been the standard of care for nearly four decades, but its efficacy and safety in children remain poorly substantiated due to critical biases in historical studies and the absence of modern paediatric randomised trials. We report a toddler with severe, virologically-confirmed LF who survived without ribavirin, challenging prevailing emphasis on the drug-centric paradigm and argues for stronger policy focus on intensive supportive care. A previously healthy 20-month-old Nigerian female toddler presented with one-week history of fever, vomiting, severe respiratory distress (SpO₂ 88% on room air), and clinical signs of heart failure. Admission haemoglobin was 13.3 g/dL, thrombocytopenia (90,000/μL), marked leukocytosis with neutrophils predominant. Lassa fever was suspected only after clinical deterioration and later confirmed by RT-PCR. Ribavirin was not administered because of delayed suspicion, delayed molecular confirmation and supply constraints. She was managed exclusively with intensive supportive care: supplemental oxygen, sequential broad-spectrum IV antibiotics, antiemetics, cautious fluid resuscitation, diuretics and nutritional care. On day 13, her father requested discharge against medical advice (DAMA) as she appeared fully recovered. A delayed RT-PCR returned positive for Lassa virus three days later. Four-week follow-up confirmed sustained good health. This case adds to emerging evidence that survival of severe pediatric LF is achievable with intensive supportive care alone, addressing clinical and physiological derangement early and intensively. Compared to previously published pediatric LF survivors (all received ribavirin), our patient had comparable disease severity but no drug-related anemia. The 5-day diagnostic delay, while a serious challenge, created a natural experience demonstrating that life-saving supportive care need not await virological confirmation. Diagnostic delay and parental anxiety leading to DAMA are common challenges in resource-limited settings and must be addressed through decentralized rapid diagnostics and structural family counselling.

Keywords: Diagnostic delay, Heart failure, Ribavirin, Supportive care, Respiratory distress, Paediatric Lassa fever

INTRODUCTION

Lassa fever (LF), a viral haemorrhagic fever caused by the Lassa virus (LASV) and transmitted primarily by *Mastomys natalensis* rodents contaminating food, household items or the environment, is endemic to West Africa.^{1,2} Human-to-human and healthcare-associated transmission can also occur, especially where infection-prevention systems are fragile.^{3,4} Nigeria bears a disproportionately heavy burden; between January and May 2026 alone, the Nigeria Centre for Disease Control and Prevention (NCDC) reported 4,861 suspected cases and 191 confirmed deaths, with a CFR of 25.2% - significantly higher than the 18.5-19.1%

recorded during the same period in 2025.^{5,6} The annual infections and deaths in Nigeria remain estimated at 300,000–500,000 and over 5,000 respectively.^{1,2} Children under five years are particularly vulnerable, often presenting with non-specific febrile illness causing diagnostic ambiguity, late presentation, communicate symptoms poorly and may rapidly deteriorate to multi-organ dysfunction, including hemorrhage, acute kidney injury (AKI), and cardiovascular collapse before virological confirmation is available.^{6,7,8}

The mainstay for LF treatment protocol has been intravenous (IV) ribavirin for nearly four decades now, based on a landmark 1986 study by McCormick et al.

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which reported a dramatic mortality reduction from 55% to 5% when administered early.⁵ However, modern systematic reviews have rated this evidence as “very low certainty” citing critical methodological flaws, including immortal time bias and lack of confounders and absence of contemporary randomised controlled trial standard.^{6,9,10,11,12}

A systematic review commissioned by the Bristol Biomedical Research Centre concluded that “robust evidence supporting that use of ribavirin in Lassa fever is lacking”.⁶ Pharmacokinetic modelling further suggests that current ribavirin regimens achieve serum concentrations exceeding the mean EC₅₀ for less than 20% of the time and the mean EC₉₀ for less than 10% of the time, raising serious questions about whether the drug reliably inhibits LASV replication *in vivo*.¹³ These debates are reason to strengthen clinical trial infrastructure and to define supportive care more explicitly as a measurable intervention.

The evidence base for ribavirin in children is even less clear. A 2024 prospective Nigeria cohort (LASCOPE) reported a low case-fatality rate (CFR) of only 2.9% for children over 12 months, all receiving ribavirin.⁶ The authors themselves questioned whether this favourable outcome reflected the drug's efficacy or the intensive supportive care provided at the tertiary centre.⁶ In contrast, a 7-year retrospective study from Sierra Leone found no significant association between ribavirin and pediatric survival ($p=0.916$).¹⁴ Also, ribavirin's known toxicities, particularly dose-dependent hemolytic anemia, could worsen the severe anemia already common in pediatric LF patients (affecting up to 42%).^{6,7}

On the basis of diagnostic uncertainty and fragile evidence, the Lassa fever landscape is still rapidly evolving. In May 2025, the INTEGRATE platform trial began enrolling patients at the Federal Medical Centre Owo, Nigeria, with the primary objective of comparing novel investigational products - including ARN-75039, favipiravir, and dexamethasone - against ribavirin for prevention of death or organ failure.¹⁵ Most recently, the first randomised controlled trial comparing favipiravir with ribavirin, published in *Nature Medicine* (May 2026), reported a hazard ratio for mortality of 0.50 in the favipiravir arm - a result that has catalysed urgent discussions about the future of LF therapeutics.¹⁶ Simultaneously, the WHO continues to call for early diagnostic tests for LF, noting that many lives could be saved if rapid diagnostics were as readily available as those for malaria and HIV.^{17,18} Also, the search for better antivirals should proceed, but this cannot substitute for oxygen, monitoring, fluids, renal support, safe transfusion, nutrition, infection prevention and family-centred communication.³

This report describes a 20-month-old toddler with virologically confirmed severe Lassa fever complicated by respiratory distress and clinical heart failure who survived without ribavirin, but supported exclusively by intensive care. This does not in any way undermine the importance of ribavirin, but rather, it is presented as a clinically instructive observation from a resource-constrained setting: highlighting the potential of supportive care as a primary determinant of survival (decisive factor separating recovery from death) and addresses the real-world challenges of diagnostic delay and parental anxiety leading to DAMA. The report follows the structure recommended

for transparent clinical case reporting.

CASE PRESENTATION

Patient information and presenting features

A 20-month-old previously healthy female from a peri-urban community in Benue State, Nigeria, was referred to our tertiary care paediatric ward with a week complaint of high-grade fever (39.2°C), non-productive cough, fast breathing, and vomiting. She had received oral artemisinin combination therapy and IV ceftriaxone/gentamicin elsewhere without improvement. No significant past medical or family history. Both parents were primary caregiver.

On admission, she was acutely ill-looking and febrile. She had severe respiratory distress with respiratory rate of 68 cycles per minute, subcostal and intercostal recessions and oxygen saturation of 88% on room air. Bilateral coarse crepitations was present. She was tachycardic at 168 beats per minute, with a gallop rhythm, tender hepatomegaly measuring 4 cm below the costal margin. Moderate pallor was noted, but no petechiae, mucosal bleeding or overt haemorrhage. The initial working diagnosis was severe bronchopneumonia with congestive heart failure.

Diagnostic assessment:

Initial laboratory investigations showed haemoglobin (Hb) 13.3 g/dL, white blood cell count (WBC) $15.1 \times 10^3/\mu\text{L}$, platelets $90 \times 10^3/\mu\text{L}$, aspartate aminotransferase (AST) 210 IU/L, alanine transferase (ALT) 145 IU/L, creatinine 0.9 mg/dL. Urinalysis revealed no protein and blood. Malaria rapid diagnostic test was negative.

On day 8 of admission, following protracted vomiting, weakness, a contact history with a confirmed LF patient was elicited. Blood was sent for Lassa virus RT-PCR at a reference laboratory, and patient was isolated while other supportive treatment continued. The differential diagnosis considered included severe bacterial sepsis, bronchopneumonia with congestive cardiac failure, malaria, viral hepatitis, and Lassa fever.

Therapeutic intervention and outcome

No IV or oral ribavirin was administered throughout the admission. The reasons were low clinical suspicion, diagnostic delay and supply constraints as there was no on-site molecular confirmation. Management consisted of supportive care bundle that included: nasal oxygen 2-4 L/min during the early critical phase, cautious intravenous fluid therapy, intravenous furosemide 2 mg/kg stat, then 1 mg/kg/dose 12hourly for 72 hours, broad spectrum antibiotics, antiemetics, nasogastric tube feeding with fortified pap or F100 equivalent.

By day 7, the fever and the respiratory distress had resolved. On day 8, vomiting and body weakness recurred; ciprofloxacin was substituted for the initial antibiotic regimen while isolation and supportive care were continued. She improved steadily, and on day 13 her father requested DAMA despite team's counselling to await RT-PCR for LF result. He stated: “*She is completely well and playing. We have been here for 2 weeks and had been waiting for the result for more than 5 days. I don't have any money left money.*” Two days after discharge, the RT-PCR returned positive for Lassa virus. Contact tracing was immediately initiated - family remained well and were all offered oral ribavirin in line with NCDC guidelines. At

four-week follow-up clinic visit, child was asymptomatic, active and thriving with no reported relapse or adverse event.

Table 1: Timeline of clinical events and supportive care interventions

Day	Clinical Event	Investigation/ Result	Intervention	Response
1	Fever, respiratory distress, gallop rhythm and hepatomegaly	Hb 13.3 g/dL; Platelets 90 x 10 ³ /uL; AST 210 IU/L; malaria RDT negative	Oxygen 2 -4L/min, IV Furosemide, cautious fluids, ceftriaxone plus gentamicin	Mild improvement
3	Persistent tachypnea, pallor	Repeat Hb 12.9 g/dL	Supportive care continued	Partial improvement
7	Afebrile with reduced distress	No new major abnormality documented	Continue supportive care, nutrition and monitoring	Clinical improvement
8	Recurrent vomiting and weakness; contact history elicited	Lassa virus RT-PCR sent; isolation initiated	Antibiotics changed to IV ciprofloxacin; antiemetics, and cautious fluid therapy	Gradual recovery
13	Fully active, playing; PDR pending	Result not yet available	Counselling given; father requests DAMA	Discharged against advice
15	–	RT-PCR Positive for Lassa virus	Contact tracing and family monitoring	No secondary cases
4 weeks	Well, no symptoms	Normal	None	Sustained recovery

Table 2: Differential diagnosis

Condition	Supporting features	Against
Severe bacterial sepsis/pneumonia	Fever, tachypnea, crepitations, leukocytosis	No response to broad-spectrum antibiotics
Lassa fever	Protracted vomiting, contact history, thrombocytopenia, elevated AST > ALT	No bleeding, initial recovery
Malaria	Fever, anemia	RDT negative,
Viral hepatitis	Hepatomegaly, elevated transaminases	No jaundice, normal synthetic function

DISCUSSION

We report a case of severe, virologically confirmed Lassa fever in a 20-month-old child, complicated by heart failure, and severe respiratory distress, alongside thrombocytopenia and transaminitis, who achieved full clinical recovery without receiving ribavirin. Her management relied entirely on a bundle of intensive supportive care: supplemental oxygen, sequential broad-spectrum antibiotics, cautious fluid management and cardiovascular support. This case challenges the historical ribavirin-centric paradigm and aligns with real-world possibility of survival from severe Lassa fever with high-quality supportive care alone, especially in settings where RT-PCR confirmation and antiviral access may lag behind clinical deterioration.^{3,19,20}

The Shifting Evidence Base for Ribavirin

Our findings align with recent literature questioning the necessity and supremacy of ribavirin in LF management, drawing attention to supportive care. The 2022 systematic review by Cheng et al. concluded that the evidence for ribavirin's benefit in LF is of "very low certainty" due to significant biases in the original studies.⁹ In the specific context of children, the 2024 prospective LASCOPE study in Nigeria reported an overall CFR of only 5.4% in hospitalised pediatric patients, with a CFR of just 2.9% for children over 12 months, all of whom received ribavirin.⁶ This contrasts sharply with the 20% CFR historically cited.¹ The authors themselves questioned whether this low CFR reflects the benefit of ribavirin or the intensive supportive care provided at the tertiary centre where the study took place. This case provides a contrary fact: the same severe disease, same low CFR was achieved without the drug.

Furthermore, a retrospective pediatric study from Sierra Leone explicitly found that ribavirin receipt was not significantly associated with survival ($p=0.916$).¹⁴ Given ribavirin's well-documented risk of dose-dependent haemolytic anaemia,⁹ its routine administration could have been harmful, potentially worsening tissue oxygen delivery. This case differs from both cohorts because she received no ribavirin at all; nevertheless, her recovery followed prompt oxygenation, careful fluid management, treatment of suspected bacterial co-infection, diuretics for heart failure and nutritional support. The comparison is not definitive, but it supports the argument that supportive care quality is a major confounder in observational assessments of ribavirin benefit.

Supportive Care as the True Determinant of Survival

We argue that the "supportive care bundle" is the primary driver of survival in pediatric LF, not to be considered as a mere background management. The pathophysiology of severe LF is driven by a combination of viral sepsis, capillary leak, and immune-mediated organ injury, not direct viral cytolysis, with hypoxia ($SpO_2 <92\%$) being considered a strong predictor of mortality in pediatric LF ($p=0.042$).^{4,19,20} Therefore, physiological stabilisation by maintaining oxygen delivery, perfusion, and organ function is a rational and effective strategy for care in the acute phase, as much as antiviral therapy.²¹ Recent WHO guideline has also explicitly stated that "early supportive care with rehydration and symptomatic treatment improves survival".²²

Furthermore, the Nigerian context makes this point urgent. Lassa fever treatment centres have made major progress, yet gaps in oxygen access, referral speed, isolation capacity, laboratory turnaround time, blood services and infection-prevention practice remain common across resource-limited settings.^{21,23,24} Obionu and colleagues' evaluation of infection prevention and control practices in north-central Nigeria highlights that facility-level readiness is uneven even during outbreaks.²⁵ A child with severe Lassa fever needs a system, with robust supportive infrastructures, not only a vial of antiviral medicine.

Diagnostic Delay and DAMA

The 5-day diagnostic delay in our case is a systemic failure, that remains distressingly common across West Africa, but it inadvertently became an experiment. This case therefore aligns with recent diagnostic literature showing that molecular testing remains central but insufficient when samples must travel to reference laboratories.^{26,27,28,29} It also proves that clinicians in resource-limited settings do not need to wait for a positive PCR to initiate life-saving supportive care. A syndromic approach to "danger signs" (shock, respiratory distress, severe anemia, altered consciousness) can and should be started immediately, culminating in the needed intensive supportive care. The DAMA event, while challenging, is a real-world reality in resource-poor settings where prolonged hospitalisation imposes severe financial and social strain. This case highlights how diagnostic delays exacerbate parental anxiety and contribute to DAMA, which in turn leads to underreporting of LF cases and loss of follow-up data. Decentralised rapid diagnostic tests (RDTs) could help mitigate this by providing a same-day diagnosis, as well as psychosocial support to reduce DAMA.

LIMITATIONS

As a single case report, our findings are hypothesis-generating, not generalisable. We lacked serial viral load data to assess viral clearance kinetics. The possibility of an inherently mild LASV strain cannot be excluded. However, the patient's severe clinical presentation (heart failure, severe respiratory distress and protracted vomiting) argues against a mild infection.

CONCLUSION

This case describes full clinical recovery of a 20-month-old child from severe Lassa fever complicated by heart failure and severe respiratory distress, achieved entirely without ribavirin. It provides a powerful narrative. It demonstrates that intensive supportive care - oxygen, antibiotics, and hemodynamic support - is a life-saving intervention in its own right. This case calls for reconsideration in Lassa fever policy: moving beyond a four-decade-long, evidence-poor reliance on ribavirin towards a pragmatic investment in the specialised supportive care infrastructure, shortened diagnostic delay, that truly determines survival for children in West Africa.

RECOMMENDATIONS FOR POLICY AND PRACTICE

Based on this case and the contemporary literature, we propose the following:

1. Prioritize Investment in Supportive Care Infrastructure: Funding should be directed towards ensuring the availability of medical oxygen, pulse oximeters, blood transfusion services, and basic intensive care capabilities (hemodynamic monitoring, inotropes) at all LF treatment centers.
2. Decentralize Diagnostics: Rapid, quality-assured molecular point-of-care PCR or antigen-based tests for LF are urgently needed to reduce diagnostic delays, guide infection control, and improve patient trust.^{27,28,29}
3. Conduct Rigorous Pediatric Trials: An ethical and clinical imperative exists to conduct a multi-center, randomized controlled trial (RCT) comparing ribavirin, favipiravir, or newer candidates plus supportive care versus supportive care alone in pediatric LF.^{17,18}
4. IV Ribavirin Remains Essential: For all confirmed paediatric Lassa fever cases, IV ribavirin remains the standard of care; however, we recommend incorporation of additional severity markers (e.g., high AST or viral load) to guide the intensity of supportive care and monitoring, without altering the indication for ribavirin.

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