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LASSA FEVER OUTBREAK INVESTIGATION IN TONKOLILI DISTRICT, MARCH 2022

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ABSTRACT

Background: Lassa fever is an endemic zoonotic disease in West African countries, including Sierra Leone. On March 3, 2022, Tonkolili District Surveillance Unit received notification of suspected Lassa fever cases from a hospital. The Sierra Leone Field Epidemiology Training Program (SLFETP) trainees and mentors responded within 24 hours to confirm the diagnosis, identify sources, and institute control measures.

Methods: We interviewed case patients and families using a case investigation form; reviewed patients' records; collected blood specimens and sent them to the Reference Laboratory. Environmental assessment, rodent trapping, and an active case search were conducted, and 29 contacts were line-listed and monitored for 21 days.

Result: Two suspected cases tested positive for Lassa fever. On February 25, 2022, a 5-year-old male (Case 1) developed fever, abdominal pain, and diarrhea, he was admitted to the hospital on March 1, 2022, and treated for malaria. He died on March 3, 2022, Lassa fever was suspected and later confirmed by Polymerase Chain Reaction (PCR) testing. An 8-year-old girl (Case 2) who developed skin rashes and fever on February 25, 2022, was treated with traditional herbs at home. She was admitted to the hospital on March 1, 2022, as her symptoms persisted and was treated for malaria. Two days later, Lassa fever was suspected, and the diagnosis was confirmed four days after admission. She died on the same day of laboratory confirmation. Both patients lived in the same household with no travel history. Poor environmental sanitation was observed around the patients' households. No rodents were found, and no additional cases or symptomatic contacts were discovered.

Conclusion: Two Lassa fever cases were confirmed in Tonkolili District. Late detection by healthcare workers likely contributed to the patient's deaths. We sensitized healthcare workers on the Lassa fever case definition and recommended community education on early healthcare seeking.

Keywords: Lassa fever, Disease outbreak, Zoonoses, Polymerase chain reaction, Sierra Leone.

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INTRODUCTION

Lassa fever is a severe acute viral hemorrhagic illness caused by a virus belonging to the family Arenaviridae (Khare *et al.*, 2022). The disease was first discovered in Sierra Leone in the 1950s (Shaffer *et al.*, 2021).

The virus exhibits persistent, asymptomatic infection, with profuse urinary virus excretion in Mastomys natalensis rodents, which serve as the natural reservoir (Isere, A. A. Fatiregun, *et al.*, 2018). . The primary mode of spread is from rodents to man through contact with rodent excreta or urine in food or during hunting and processing of rats for consumption (Douno *et al.*, 2021). The virus can spread from person to person, either within households during care for sick relatives or in healthcare settings (Isere, A. Fatiregun, *et al.*, 2018).

Lassa fever is endemic in West Africa, with several outbreaks recorded over the years. Outbreaks of Lassa fever have been reported in Sierra Leone, Guinea, Liberia, Nigeria, Ghana, Ivory Coast, Senegal and Mali (Isere, A. A. Fatiregun, *et al.*, 2018). The number of infections per annum has been estimated at 100,000 to 300,000, with approximately 5,000 deaths (Isere, A. A. Fatiregun, *et al.*, 2018). Since the identification of the virus in Sierra Leone, it has become endemic in the eastern province, and yearly outbreaks have been reported in that part of the country, more recently in the northern province.

Countries reporting Lassa fever other than Sierra Leone have reported lower CFRs. In 2020, a meta-analysis of 25 countries in Sub-Saharan Africa reported 29% CFR for Lassa fever patients (Kenmoe *et al.*, 2020). In several recent Lassa fever outbreaks in Nigeria, it was estimated that between 19.5% and 22.7% of confirmed Lassa fever cases died (Cadmus *et al.*, 2023). In the early 1970s, CFRs for Lassa fever were 38% among hospitalized patients in Sierra Leone (Shaffer *et al.*, 2021). More recently, CFRs for Lassa fever have reached 69% in Sierra Leone and exceeded 80% in third-trimester pregnancies (Bell-Kareem and Smither, 2021). Another study conducted in Sierra Leone revealed Lassa fever CFRs of 67% among hospitalized patients and 63% in hospitalized children (Samuels *et al.*, 2021).

On November 20, 2019, an outbreak of Lassa fever was confirmed at Masanga Hospital in Tonkolili District. The initial case involved an expatriate surgeon and his assistant who worked at Masanga Hospital. They were repatriated to their home country and tested positive for Lassa fever, the surgeon later died and the assistant survived (Njuguna *et al.*, 2022). The two doctors had performed surgery on a 30-year-old and 33-year-old pregnant women. These women admitted at Masanga Hospital were from the Mayero community in Simiria Chiefdom and the Sasakla community in Kalansogia Chiefdom, respectively. In November 2019, both women died from symptoms similar to Lassa fever. No blood samples were collected, but the district health management team classified the two women as probable Lassa fever cases, with a case fatality rate of 60% (Njuguna *et al.*, 2022)

On March 3, 2022, the District Health Management Team (DHMT) was also notified by Masanga Hospital of two suspected cases of Acute Viral Hemorrhagic fever (AVHF). A joint team from the DHMT and Sierra Leone Field Epidemiology Training Program (SLFETP) deployed immediately to respond, collect samples, and line list cases. Therefore, we

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aimed to confirm and describe the existence of the outbreak and identify the aetiology.

METHODS

Outbreak setting

The outbreak was reported from the Matapi community in Simiria chiefdom, one of the nineteen chiefdoms in the Tonkolili District. Tonkolili District is one of the sixteen districts located in the Northern region of Sierra Leone. The district shares boundaries with seven districts: Bombali, Kono, Kainadugu, Port Loko, Bo, Kenema, and Moyamba. The projected population of the district for 2022 is 636,578 from the 2015 population and housing census projection report. In this district, a confirmed case of Lassa fever is considered an outbreak, while any suspected case should be investigated. The district has 104 health facilities: three hospitals, 14 Community Health Centers (CHC), eight Community Health Posts (CHPs), and 82 Maternal and Child Health Posts (MCHP). Simiria Chiefdom has four peripheral health Units (PHU), one community health centre, and three maternal and child health posts.

Population

Outbreak Support Techniques

The FETP team, upon arrival, convened an emergency meeting with the District Health Management Team (DHMT) and conducted a strength, Weakness, opportunity, and Threat (SWOT) analysis of the response and provided support on the investigation by visiting the Matapi village, active case search by visiting PHU and reviewing records and help inline listing of contacts.

Outbreak Case Definition

We have developed the following working case definitions to assist investigation team members easily identify cases.

Suspected case: Any person with fever (≥37.5^{0}C) and two or more of the following symptoms: malaise, sore throat, cough, vomiting, diarrhoea, myalgia, chest pain, hearing loss, or unexplained death from Kafe and Simiria chiefdoms from March 1 to 31, 2022.

Probable case: Any person whom the clinician suspects of having Lassa fever but is unable to confirm using laboratory tests or any suspected case who has died and has an epidemiological link to a confirmed case

Confirmed case: Any person Suspected /Probable case with positive laboratory result by enzyme-linked immunosorbent assay (ELISA) or real-time polymerase chain reaction (RT-PCR).

Contact: A person without any symptoms having had physical contact (direct or indirect) with a confirmed case or the body fluid of a case or has had contact with any person who died of Lassa fever within the last three weeks.

Laboratory diagnosis

Laboratory confirmation was conducted at the Lassa Fever Laboratory in Kenema District, Sierra Leone. This facility is a Tulane reference laboratory specializing in Lassa fever diagnosis, treatment, and research. The confirmation was based on a positive test using Lassa virus-specific RT-PCR. Laboratory samples (8 ml of serum) were collected from each suspected case identified during the investigation. These samples were packaged in triplicate and

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transported to the laboratory using the reverse cold chain system by trained laboratory personnel. Feedback was provided to the district within 48 hours.

Environmental assessment and rodent trapping

We went through the community and observed the status of waste management and environmental conditions. The Lassa fever surveillance team from Kenema set up 35 rodent traps at the Matapi Village for 22 hours, starting at noon and ending at 10:00 a.m. the following day.

Contact tracing and active case search

We conducted contact tracing, identifying and line-listing contacts, and followed up for 21 days after their last contact with the case. Contacts were classified as high-risk and low-risk. Blood samples were collected from the high-risk contacts to determine the presence of the virus before the end of the incubation period. The team visited Masanga Hospital and other peripheral health units in the Simiria Chiefdom community to conduct an active case search. Registers from February 25 to March 14, 2022, were reviewed for suspected cases meeting the Lassa fever case definition. Questions were asked to clarify a few cases with signs and symptoms related to Lassa fever, but no suspected cases were identified from the register.

Data collection technique and design

We used the national surveillance case investigation form for viral hemorrhagic fever to collect information from suspected cases and contacts. A case series descriptive analysis was conducted.

RESULTS

Cases presentation

Lassa fever outbreak was confirmed in Mathapie village, Simiria Chiefdom, Tonkolili district, with two cases and 29 contacts identified during the investigation. Case 1 involves a 5-year-old boy from Mathapie village, Simiria Chiefdom, Tonkolili District, with no travel history. He fell ill on February 25, 2022, with a fever, as reported by his parents. Initially treated at home, his condition worsened, and he was taken to Masanga Hospital on March 1, 2022. Upon admission, he presented with fever, vomiting, diarrhea, muscle pain, abdominal pain, and difficulty breathing. The clinicians at Masanga Hospital tested him for malaria, which came back positive. Despite treatment, his condition deteriorated, and he was admitted to the pediatric ward for observation, where he died on March 3, 2022.

His death heightened suspicion of Viral Hemorrhagic Fever (VHF) infection, prompting the hospital to notify the district surveillance team immediately. Upon the team's arrival with laboratory staff, a sample was collected and sent to the Tulane reference lab in Kenema District on March 3, 2022. The sample initially tested negative for Ebola but later tested positive for the Lassa virus (LASV). The District Health Management Team (DHMT) received the laboratory results from the reference laboratory through the district surveillance officer on March 5, 2022, after the boy's body had been released to his family.

Case 2 is an 8-year-old girl from the same village and chiefdom as Case 1; she is his sibling. She began developing a rash with a mild fever at the beginning of February 2022. She did not seek medical attention and was instead treated with a traditional medicine ointment. A

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few weeks later, the rash reappeared with new, worsening symptoms. Like her brother, she had no travel history and became seriously ill on February 27, 2022, two days after Case 1 started showing symptoms.

Case 2 exhibited fever, vomiting, diarrhea, extreme fatigue, and difficulty breathing. On March 1, 2022, she was taken to Masanga Hospital along with her brother. She was admitted to the pediatric ward and treated for malaria, but her condition did not improve. Due to her brother's death, the clinicians suspected Lassa fever. On March 3, 2022, blood samples and a swab from Case 1 were sent to the Tulane reference lab in Kenema for testing. The hospital notified the Tonkolili surveillance team about the suspected case. The test results came positive on March 5, 2022. On that note, the case was finally transferred to the Kenema Lassa Fever Treatment Centre for antiviral treatment on March 6, 2022. The case died before reaching the hospital, and her burial was performed by the Lassa fever team in Kenema.

4.1 **Contact tracing findings**

All 29 contacts identified were line-listed and followed up for twenty-one days after the last date of contact with the case. Of the 29 contacts, five were from Matapi Village, 21 were staff at Mansaga Hospital, and three were from pediatric inpatient wards where cases were admitted. Moreover, five (17%) of the 29 contacts were classified as high-risk and twenty-four (83%) as low-risk contacts. Blood samples were collected from the high-risk contacts to determine the virus's presence before the incubation period's end. However, none of the contacts showed any signs or symptoms of Lassa fever after the 21-day follow-up. The five high-priority contacts were tested, and the results came out negative for the Lassa fever virus.

4.2 **Active case search**

The team visited Mansaga Hospital, other peripheral health units, and communities in the Simiria chiefdom to conduct an active case search. Registers from February 25 to March 14, 2022, were reviewed for suspected cases meeting the Lassa fever case definition. Questions were asked to clarify a few cases with signs and symptoms related to Lassa fever, but no suspected cases were identified in the register.

4.3 Environmental and Infection Prevention and Control (IPC)Measures/ Health Education

The investigation team visited the community and observed that the Mathapie village is a small community surrounded by plantations with no proper waste management that can lead to the breeding sites of rodents. There was a limited supply of Infection Prevention and Control (IPC) materials at Mansaga Hospital, which exposed the healthcare worker to a high risk of nosocomial infection. There was breach in IPC by healthcare workers at Mansaga Hospital and a dirty environment that led to general cleaning by the IPC national team. We orientated the health workers on Lassa fever prevention, the use of Personal Protective Equipment (PPE), hand hygiene practices, and waste management procedures; we also printed brochures and shared them with health workers at Masanga Hospital. Furthermore, we sensitized the community people on Lassa fever prevention and control. We pasted out flyers on households, distributed brochures to community informants, orientated community health workers to do house sensitization on the

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prevention and control of Lassa fever using the flyers, and also had an interactive radio discussion.

DISCUSSIONS

This investigation aimed to confirm and describe the existence of the Lass fever outbreak and identify the aetiology. Two cases of Lassa fever were identified and confirmed in Masanga Hospital from Matapi Village in Tonkolili District, located in Northern Sierra Leone. The two cases were siblings of a 5-year-old male and an 8-year-old female, and both cases died.

From the study, we observed a late diagnosis of Lassa fever at Masanga Hospital as both cases were suspected of malaria infection, even though one case was positive for malaria. This led to worsening their clinical condition, which could be the cause of death. The situation is complicated by the possibility of co-infection. One of the patients in the study tested positive for malaria, which likely reinforced the initial diagnosis. This co-infection can obscure the presence of Lassa fever, delaying the correct diagnosis and appropriate treatment. It is crucial to consider the possibility of multiple concurrent infections in such settings. Clinicians, particularly in malaria-endemic settings, will find it difficult to suspect Lassa fever as it has similar symptoms to malaria as well as several other tropical diseases. A study conducted in Sierra Leone reported late diagnosis of Lassa fever, particularly in endemic countries, can lead to high mortality. The same study reported that late detection of Lassa fever in two children infected with the disease might be the cause of their death (Sesay et al., 2022). So, it is necessary for clinicians working in Lassa-endemic countries to consider the disease in their differential diagnosis. The US Center for Disease Control and Prevention (CDC) reported that about 10 - 16% of annual hospital admissions are due to Lassa Fever in Sierra Leone and Liberia (Centers for Disease Control and Prevention, 2022).

Differential diagnosis and case definitions are essential and can lead to a late diagnosis of Lassa fever. A study conducted in Sierra Leone to assess the systemic and structural barriers to detecting and responding to Lassa fever identified several challenges that can lead to late diagnosis. These challenges included Lassa fever case definition, approaches to differential diagnosis, specimen transportation, and case management (Rohan, 2022). The death of the two cases in this study could be attributed to the late seeking of medical care and detection of Lassa fever cases, which led to the worsening of their clinical condition. A study conducted in Sierra Leone indicated that among untreated laboratory Lassa fever confirmed cases, 87% had a chance of death (Dahmane et al., 2014).

This investigation observed that one Lassa fever case was co-infected with malaria. This could be attributed to the effect of Lassa fever on the immunity system makes the patient exposed to other diseases. Studies indicated that the Lassa fever virus causes generalized immune suppression of both innate and adaptive immune responses. Lassa fever targeted both macrophages and dendritic cells at the early stage of the infection (Walker et al., 1975; Lukashevich et al., 1999; Mahanty et al., 2003). This could lead to the high prevalence of Lassa fever and malaria co-infection. A study conducted to assess the impact of malaria on the Lassa fever outcome found a high

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prevalence of co-infection (37%) with malaria in patients with Lassa fever infection (Okokhere, Asogun and Okogbenin, 2010).

Both Lassa fever cases in this investigation did not have any travel history within the last three weeks before their illnesses. Although we were not able to identify the source of infection in this investigation, the Lassa fever infection might have happened through direct contact with an infected rodent or indirect contact with the urine of infected rodents. Additionally, the first case might have been infected in the community, and infected the second case through human-to-human transmission. A study conducted in Liberia showed that the Lassa fever cases did not have a travel history and attributed the Lassa fever infection to the conduct with infected rodents or indirectly through exposure to rodents' urine or droppings (Woyessa et al., 2019). Based on this investigation, the 8-year-old girl was seeking traditional medication before seeking medical care. This might contribute to a delay in seeking medical care and eventually worsening the condition of this case. A study conducted in Nigeria reported the index case that causes nosocomial infection was taken to a herbalist where he spent five days before seeking medical service leading to worsening clinical conditions (Cc et al., 2019).

Our investigation discovered that the death of the two patients who died of febrile illness was a result of an underlying causative agent associated with the Lassa fever virus and the two diseased cases were reported from the same place with no epidemiologic linkage between the two cases.

Although the environmental assessment was conducted, the team was not able to capture any rodents in the household and community where these two cases were residing. Catching rodents could help in identifying the source of infection if the Lassa fever virus is isolated from it

Limitation

A possibility of recall bias may occur; the accuracy of the information collected from questioning could be affected by the inability of respondents (cases and contacts) to accurately recall events or symptoms. Moreover, there was limited geographic scope during the investigation. The investigation focused on Masanga Hospital and nearby health units in Simiria Chiefdom. Cases in other regions or those who did not seek medical help might have been missed.

Conclusion

This investigation confirms Lassa fever infection in two cases in Tonkolil District, Sierra Leone. Both cases died and no source of infection was identified. We recommend initiating community sensitization to follow preventive measures such as controlling rodents from entering the household. Communities to maintain good sanitation measures to avoid breathing sites of rodents. Also, we recommended clinicians increase the index suspicion for Lassa fever and consider it in their differential diagnosis. We recommend timely blood sample collection and release of the result for better case management.

Authors' Contributions: MSB, Alieu Tommy, Zainab Juhehbah and Kassim Kamara were involved in all aspects of this report including conceptualization, study design, data collection, statistical analysis, and manuscript writing. AHE, SAS, and GNG, contributed to the

analysis and substantially reviewed the manuscript. All authors approved the final manuscript.

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Competing interests: All authors disclose no conflicts of interest whatsoever.

Availability of data and materials: The dataset is available through the corresponding author upon reasonable request.

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Annexes

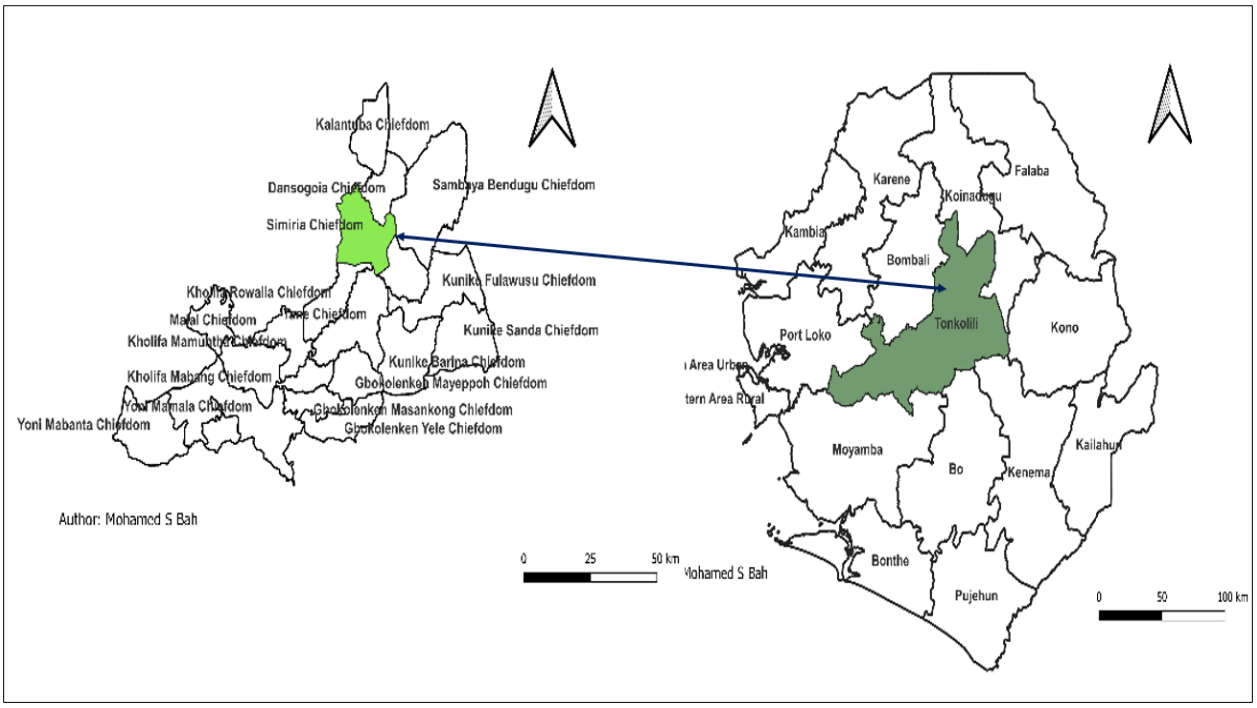

Figure 1: ***Map of Sierra Leone showing map of Tonkolili where the cases were reported, March 2022***