

## Psychiatric Symptoms in People with Probable or Confirmed Lassa Fever in a Military Hospital in North Central Nigeria: A Case Series

Obekpa Isaiah Obekpa<sup>1</sup>, Godian Chibueze Ezema<sup>2</sup>, David Tariemi Adika<sup>2</sup>, Oluwagbogo Christiana Oyebade<sup>2</sup>, Olatunji Samuel Oguntuase<sup>2</sup>, Joseph Hassan Solomon<sup>2</sup>, Saheed Olawale Mustapha<sup>2</sup>, Onyemocho Audu<sup>3</sup> and Michael Agbo Amedu<sup>1</sup>

<sup>1</sup>Department of Psychiatry, Federal University of Health Sciences, Otuokpo, Benue State, Nigeria. <sup>2</sup>161 Nigerian Air Force Hospital, Makurdi Benue State, Nigeria. <sup>3</sup>Department of Public Health, Federal University of Health Sciences, Otuokpo, Benue State, Nigeria.

### ABSTRACT

Lassa fever (LF) is an important public health disease in West Africa, where it is endemic. The early phase of the disease is characterised by non-specific symptoms mimicking malaria and other common febrile illnesses. Neuro-psychiatric symptoms are not commonly reported and psychiatrist are not usually part of the management team. Surviving Lassa fever patients with psychiatric symptoms tend to have long hospital stay. The study is aimed at describing the pattern of neuro-psychiatric symptoms in people with probable or confirmed Lassa fever at the 161 Nigerian Air force Hospital (NAF), Makurdi. Neuro-psychiatric symptoms were common in patients with probable or confirmed Lassa fever. Delirium, low mood and convulsions were common in the series. There is need for more research on the psychiatric aspects of Lassa fever and the involvement of psychiatrists in treatment could improve the outcomes of patients with Lassa fever.

**Keywords:** Lassa fever; psychiatric symptoms; Nigeria.

### INTRODUCTION

Lassa fever (LF) is a re-emerging viral haemorrhagic fever (VHF) caused by the single stranded RNA Lassa Virus, which belongs to the virus family of Arena Viridae. [1] Lassa fever is an important public health problem that is endemic in West Africa affecting 300, 000 to 500, 000 people. [2, 3] It is associated with significant morbidity, mortality and a near never-ending circle of challenges like few treatment centres, [2-4] absence of dedicated dialysis machines, poorly maintained isolation and treatment units amongst others.

The symptoms of Lassa fever are non-specific in the early phase. The categories [4] are: An alert case in which a person has unexplained fever with or without bleeding. [4] A suspected case is defined as a patient with fever for 3-21 days with a measured temperature of 38°C or more with one or more of the following: vomiting, diarrhoea, sore throat, myalgia, generalised body weakness, abnormal, abdominal pain. [4] Probable case is defined as a suspected case with one or more of the following complications: Hearing loss, facial or neck swelling, seizures,

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##### \*Correspondence:

Obekpa Isaiah Obekpa.  
Department of Psychiatry  
Federal University of Health  
Sciences  
Otuokpo, Benue State.  
Tel: +234803 634 5170  
Email: obekpaoyi@gmail.com.

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restlessness, confusion, hypotension, oliguria, abnormal bleeding.

To the best of the authors' knowledge, only two studies in West Africa described psychiatric symptoms in people with Lassa fever. [5, 6] This study is important in contributing to knowledge on the psychiatric aspects of Lassa fever. Reported neuro-psychiatric symptoms of Lassa fever in the literature include restlessness, confusion, seizures and coma.[4-6]

Neuro-psychiatric symptoms occur late in the disease.[6-10] The presence of neuro-psychiatric symptoms in the later stages of the disease could imply a more severe disease with possible implication for grading when designing diagnostic and treatment guidelines. The only mention of neuro-psychiatric syndrome in the current national guidelines for Lassa fever case management in Nigeria [4] is encephalopathy. The document is silent on other common psychiatric symptoms like mood symptoms, auditory and visual hallucinations. The guidelines spelt out specifically how seizures are to be managed. [4] In practice, psychiatrists are not routinely part of the management team for patients with Lassa fever.

Lassa fever is a dreaded infectious disease and mortality ranges between 15-65% among hospitalised patients. [11-16] Hence the understandable psychological response of fear, confusion and anxiety among patients and hospital workers on suspicion of a case. The situation becomes complicated with the development of psychiatric symptoms like restlessness, delirium, psychosis, aggression, uncooperative attitude and outright refusal to be isolated and treated in extreme cases. Unfortunately, the much needed hands for physical and or chemical restraints at such chaotic times, to stabilize the patient and limit the spread of the infection is often lacking compared to when psychiatric symptoms are not present.

Eighty percent [80%] of cases of Lassa fever are asymptomatic. [11-15] such individuals, rather than being isolated, go about their normal activities and possibly infecting other persons.

Experiences show that patients suffering from

infectious diseases with high case fatality rates like Lassa fever often suffer neglect from HCWs in many hospitals in Nigeria due to lack of adequate personal protective equipments (PPEs), poor motivation and working conditions, leaving the patients in a bad state for the few attending HCWs. [17] This reactions by HCWs fall within the spectrum of 'germ panic.' [17]

A key successful aspect of management of LF is urgent laboratory confirmation and early commencement of intravenous ribavirin, which is known to reduce mortality from 55% to 5%. [18, 19] Again this study is important for the reason that in our environment, not much is reported of the experience of early initiation of presumptive intravenous ribavirin following only clinical suspicion of LF as is the case for antimalarial in children and pregnant women; [20] empirical antibiotics for some infections, especially around the head and neck region, before laboratory confirmation of the infection. [21]

In West Africa, [22, 23] febrile illnesses are widely treated with antimalarial and antibiotics at home, neighbourhood kiosks and drug shops, because malaria is endemic and due to a widespread belief that febrile illness is either due to malaria, typhoid or both. Similarly, the symptoms of uncomplicated malaria, typhoid and early phase of LF are similar and non-specific. This widely held traditional health beliefs and practices about malaria and typhoid, even amongst HCWs makes clinical suspicion of LF unlikely and delays timely evaluations and interventions during early outbreaks, until the number of deaths begins to rise. Often blood samples of suspected cases are transported several kilometres away from the point of treatment for laboratory confirmation only for results to arrive days after the patients have improved, deteriorated or died. It is not uncommon to have blood samples in transit or results misplaced due to logistic challenges.

The aim of this study is to describe the pattern of psychiatric symptoms in people with suspected or confirmed Lassa fever at the 161 NAF Hospital, Makurdi.

We report our experience of managing neuro-psychiatric symptoms in four out of seven cases, who

were admitted for suspected Lassa fever at the 161 Nigerian Air force Hospital (NAF), Makurdi between 1<sup>st</sup> November 2020 and October 30<sup>th</sup>, 2021. All patients with suspected or confirmed LF were included in the study. The information obtained from the patient files were entered into a questionnaire designed by the researchers, coded and analysed. Approval was received from the Health Research Ethics Committee of the Ministry of Defence, Abuja before the study was conducted. (MODHREC/APP./0/5/3 Date: /0/7/1/0/20/2/1/NHREC/28/01/2020B)

We describe only the cases with neuro-psychiatric symptoms:

## DESCRIPTION OF CASES

### Case one

A 30-year old male military personnel presented with high grade fever (38<sup>o</sup>C), generalised body weakness, abdominal (epigastric) pains, vomiting, passage of loose stools, and tenderness in both right and left iliac fossae. His psychiatric symptoms include irrational talks and behaviours, Confusion, restlessness, sleep disturbances and weeping spells. His blood sample taken for Polymerase Chain Reaction (PCR) test for Lassa fever was misplaced in transit to Irrua Specialist Teaching Hospital in Edo State, Nigeria and so he had no LF result. However, intravenous ribavirin was commenced on the 3<sup>rd</sup> day of admission since he satisfied the criteria for a suspected case of Lassa fever. He made dramatic and uneventful recovery and was discharged on the 16<sup>th</sup> day on admission.

### Case two

A 36-year old housewife presented with high grade fever (39.6 <sup>o</sup>C), chest pain, abdominal pain (epigastric), headache, vomiting, generalised body weakness, painful urination, frequent urination, passage of loose stools. Psychiatric symptoms include hearing voices, not heard by others in clear consciousness, restlessness and sleep disturbances. She was commenced on intravenous ribavirin on the 6<sup>th</sup> day of admission while awaiting result of PCR for

LF, which later turned out to be positive. She made uneventful recovery and was discharged on the 23<sup>rd</sup> day of admission.

### Case three

A 52-year old female military personnel presented with high grade fever (38.8<sup>o</sup>C), generalised body pains and weakness, vomiting, passage of loose stools, epigastric and hypochondriac pains. Neurological symptoms include headaches, convulsions and loss of consciousness. Psychiatric symptoms include irrational talks and behaviours, confusion, restlessness, sleep disturbances, low mood and perceiving smell not perceived by others in clear consciousness. She had co-morbid peptic ulcer disease, Chronic Obstructive Pulmonary Disease, Hypertension and diabetes. Intravenous ribavirin was commenced on the 4<sup>th</sup> day of admission because she had contact with her husband (**Case 2**), who was managed and discharged few days earlier for LF in the same centre. Her PCR test for Lassa fever was positive. She had Tablet Haloperidol 5mg two times daily and Tablet Propranolol 20mg two times daily. She made good recovery and was discharged home after 32 days on admission.

### Case four

A 5-year-old female child who presented with high grade fever (38.4<sup>o</sup>C), vomiting, abdominal pains, generalised body pains and weakness. She had neurological symptoms of convulsions and loss of consciousness. She developed gangrenous spots behind her ears, ear lobes and left heel. There was also passage of loose dark coloured stools and difficulty in breathing. Intravenous ribavirin was presumptively commenced on the 2<sup>nd</sup> day of admission after blood sample was taken for Lassa fever PCR. The PCR result was reportedly missing. She also had blood transfusion, fluids and other supportive treatments. She made good recovery and was discharged on the 17<sup>th</sup> day of admission.

## DISCUSSION

Neuro-psychiatric symptoms were generally

common in the case series. Four (57.1%) out of a total of seven patients had probable or confirmed Lassa fever with neuro-psychiatric symptoms.

The commonest symptoms in the case series were delirium, auditory hallucinations, low mood and convulsions. Less common symptoms include irrational talks and olfactory hallucinations. Two out of all four patients with neuro-psychiatric symptoms had symptoms in keeping with delirium. These include confusion, psychomotor disturbance, sleep difficulties, hallucinatory experiences. Although there is dearth of data on the psychiatric aspects of Lassa fever, our commonest finding of delirium is comparable to the findings in Sierra Leone and Nigeria [5, 6] Infections seeding to the brain through various means is commonly associated with delirium. [24] This could be due to haematogenous spread, breach of blood-brain barrier and affectation of endothelial cells through infected leucocytes. [25, 26] Also, dehydration, deranged serum electrolytes, urea, creatinine, medications and impaired liver function are known causes of delirium. The average length of hospital stay for patients with neuro-psychiatric symptoms in this study was twenty two (22) days compared to sixteen and a half (16 1/2) day for the patients without neuro-psychiatric symptoms. Although only two of the patients had delirium, patients with infectious disease and delirium are known to have prolonged hospital stay [27, 28] Evidence indicates that neuro-psychiatric symptoms tend to occur late in the course of Lassa fever [6-10] This implies a possible association between Lassa fever, neuro-psychiatric symptoms and prolonged hospital stay for surviving hospitalised patients. Of the four cases, three are females, while one is a male. Of the four cases, three are adults while one is a child. This is consistent with evidence that Lassa fever occurs in both males and females and in people of all ages. [4]

Only one patient received Haloperidol 5mg B.D and Propranolol 20mg B.D. and psycho-education. The other three patients with neuropsychiatric symptoms received only supportive psycho-education. All four patients received intravenous ribavirin and supportive medical interventions like fluid and

electrolyte corrections. One patient (the 5 year old child) had blood transfusion.

Lassa fever is a common cause of febrile illness in West Africa, though clinical diagnosis by medical practitioners remains poor during early outbreaks. [29] Unlike Malaria which tends to have a near constant prevalence all year round, the outbreaks of Lassa fever occurs mostly in the dry months of October to April, with the disease nearly almost skipping some dry seasons in the sub-region. These seasonal outbreaks, near absence of the disease for some years, re-emerging nature, coupled with the non-specific symptoms of the disease in the early phase and unavailability of virology laboratory for confirmation, all account for the poor clinical diagnosis of the disease amongst medical practitioners.

In Nigeria, Okogbeni et al reported 8.8% prevalence of neuro-psychiatric manifestations among patients with LF. Delirium, depression were the commonest [5] Earlier in Sierra Leone, a rate of 30% was reported for psychiatric symptoms [6] In this study, we report a rate of 57% of neuro-psychiatric symptoms. The higher rate in our study is likely due to differences in sample size and study design. Our study recruited probable and confirmed cases of Lassa fever, while the Irrua study recruited only confirmed cases. Another possible reason is the increased recognition abilities for psychiatric symptoms by non-psychiatrists working closely with the visiting consultant psychiatrist in this military health facility in a Consultation Liaison Psychiatric (CLP) service. None of the 4 patients had a past history of psychiatric illness, making the presence of LF to explain their neuro-psychiatric symptoms.

All surviving patients had intravenous ribavirin commenced earlier than 9 days (2-6 days), even without PCR confirmatory result for Lassa fever. This treatment strategy proved to be beneficial as the remaining 6 cases survived the disease while awaiting results of PCR for LF. The pattern of clinical presentation of all the patients was fairly consistent. Once the managing team noticed the symptom cluster of fever, vomiting, epigastric pains coupled with deranged serum Electrolytes, Urea, Creatinine

(E/U/Cr), Liver Function Tests (LFTs), intravenous ribavirin was commenced. Evidence had stated that commencement of intravenous ribavirin reduces mortality in LF from 55%-5% among hospitalised patients [19] when commenced within the first 6 days.

The average length of hospital stay for cases without neuro-psychiatric symptoms is sixteen and a half day, while it is twenty two days for cases with neuro-psychiatric symptoms. The longest hospital stay was 32 days. She had delirium which is associated with prolonged hospital stay. She also had other comorbidities like hypertension, diabetes, chronic obstructive pulmonary disease and peptic ulcer disease which possibly contributed to her prolonged hospital stay

## CONCLUSION

Neuro-psychiatric symptoms in people with probable or confirmed Lassa fever are common, affecting all ages and sex and tend to be associated with later stages of the disease and prolonged hospital stay. Routine psychiatric assessments and interventions for suspected and confirmed cases of Lassa fever and further research on the psychiatric aspects could improve the outcome of patients with Lassa fever.

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## Author contribution

Obekpa Isaiah Obekpa, Godian Chibueze Ezema, David Tariemi Adika, Oluwagbogo Christiana Oyebade conceptualized and designed the study. They also contributed to implementation of the project and revision of the manuscript. All authors were involved in the writing and revision of the manuscript. The authors read, approved the final manuscript and agree to be accountable for all aspects of the work.

## Data availability

The data used to support the findings of this study are available from the site publicly.

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## Conflict of interest

None declared.

## Ethical approval

Informed consent was obtained from the patients to allow the reporting of these cases.

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