

Clinical Profile of Lassa Fever Patients in Abakaliki, South-Eastern Nigeria, January - March 2018

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Abstract

Background: Lassa fever is a zoonotic disease endemic in West Africa. Despite several outbreaks of Lassa fever in Nigeria, only few studies have been done on the clinical profile of the disease. We described the clinical profile of positive Lassa fever patients from January – March 2018 in Ebonyi state. **Methods:** We analysed the epidemiological data from the case investigation forms and clinical data from the hospital records. We did univariate analysis of the socio-demographic and clinical variables and multivariate analysis to identify the independent socio demographics and clinical factors. Statistical significance level was taken at p value ≤ 0.05 , at 95% confidence interval. **Results:** Sixty two cases were positive with mean age of 35 ± 16.2 years. The total case fatality rate was 19%, higher among health workers (31%). The case fatality rate for patients on Ribavirin was 16%. The age group mostly affected was 30-39 years and the least 0-9 years. Most were females (59.7%) and traders (26.2%), (42.9%) had tertiary level of education. Fever (78%), headache (62%), cough (38%) and were the most reported symptoms at presentation while common complications included nasal bleeding (14%) and jaundice (6%). Having abdominal pain ($p=0.0015$, $CI=0.022-0.500$) and diarrhea ($p=0.0019$, $CI=0.030-0.521$) were related with mortality while treatment with Ribavirin ($P=0.0334$, $OR=10$) was associated with survival. **Conclusion:** Diarrhea and abdominal pain were key symptoms related to mortality. Even with Ribavirin treatment, there was a high rate of fatalities underscoring the need to develop more effective and/or supplemental treatments for Lassa fever.

Keywords: Clinical; Lassa fever; Profile; symptoms; Virus; Zoonosis

Introduction

Lassa fever was first described in 1969 in the town of Lassa, in Borno State, Nigeria located in the Yedseram river valley at the south end of Lake Chad. [1] It is an acute, highly communicable viral haemorrhagic illness caused by Lassa virus, an arena virus. It is characterized by fever, muscle aches, sore throat, cough, nausea, vomiting, chest and abdominal pain as well as bleeding from the orifices. Its primary host is the multi-mammate rat (*Mastomys natalensis*), an animal indigenous to Sub-Saharan Africa and many states in Nigeria. [2] Lassa fever is transmitted to humans from contacts with food or household items contaminated with rat (*Mastomys natalensis*) faeces or urine. Person to person spread also occurs by inhalation or direct contact with blood, vomitus, urine, saliva, feces, throat secretions and other body fluids with Lassa virus. It is asymptomatic in 80% of the cases and causes severe multi-system disease, where the virus affects several organs in the body, such as the liver, spleen and kidneys in the rest. The incubation period of Lassa fever ranges from 6-21 days. [3] The signs and symptoms of Lassa fever may be difficult to distinguish from diseases that are common in the tropics such as severe malaria, typhoid fever.

Lassa fever is most often diagnosed by using enzyme-linked immunosorbent serologic assays (ELISA), which detect IgM and IgG antibodies as well as Lassa antigen. In this study, isolation of virus detected by immunofluorescent staining for viral antigen along with a positive reverse transcriptase-PCR (RT-PCR) test on the isolate was employed. Lassa virus can be isolated by laboratory cultures of blood, urine or throat washing for up to 2 weeks post onset. Other laboratory findings in Lassa fever include lymphopenia, thrombocytopenia and elevated

aspartate aminotransferase (AST) levels in the blood. Ribavirin, an antiviral drug, has been used with success in Lassa fever patients. It has been shown to be most effective when given intravenously within 6 days of symptoms.

Lassa fever is an epidemic prone disease with an alert threshold of a single suspected case and an epidemic threshold of a single confirmed case. Ever since, outbreaks of the disease have occurred in Nigeria, Liberia, Sierra Leone, Guinea and the Central African Republic. The infection is endemic in West African countries and causes 100,000 - 500,000 cases annually with about 5,000 deaths. [4] Several epidemics of Lassa fever have occurred in Nigeria. Notable outbreaks in Nigeria include: Vom Jos Plateau State (1975), Aboh Mbaize Imo State (1990), Ekpoma in Edo State (1990 & 1992), Lafia in Nasarawa State (1992-1993). Onitsha Anambra State (1994), Zonkwe (1994-1997), Abuja (2009), Kebbi (2010), Adamawa (2011) and Abakaliki (2005, 2008, 2011, 2012, 2013, 2014, 2016, 2017, 2018). [5-12] In 2012 and 2013, Nigeria recorded more than 2,900 Lassa fever cases across several states. Since early 2015 up till date, Lassa Fever outbreak has been occurring frequently in Nigeria. Between August 2015 and May 2016, the nation recorded one of the largest outbreaks of Lassa fever in its history.

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Recently, the disease has become endemic in some states in Nigeria. There were 312 confirmed cases of Lassa fever with 78 deaths in Nigeria in 2017. The pattern of the outbreak in 2017 is unique because it occurred all year round in different states; defying the usual seasonal LF outbreak pattern. In these instances, the Lassa fever outbreak has often spread to affect health care workers and within health facilities resulting in severe morbidities and mortalities.^[13] Nineteen states were affected including Ebonyi State.

Over the past ten-year period (2005-2014), Lassa fever have been recurring in Ebonyi State, with 82 cases of Lassa fever notified, 50 (61%) were suspected and 32 (39%) confirmed. The male: female ratio was 1.3: 1 with an overall case fatality rate of 30.5%. In 2016, 104 cases were recorded.^[14] The major challenge to health care providers in endemic areas are the development of rapid diagnostic tests, increasing availability of the only known drug treatment, Ribavirin and provision of materials for barrier nursing and adequate facilities for isolation of infected cases.^[15] Case reports of LF mimicking ectopic pregnancies have also been reported in Ebonyi state.^[16] Among those admitted for Lassa fever the case fatality is approximately 15%-23%.^[17] Despite the endemic nature of Lassa fever in Nigeria, the details of the outbreak investigation and the epidemiological characteristics of the cases have not been well documented.

Nigerian centre for disease control (NCDC), On the 14th January 2018, was notified of confirmed case of Lassa fever of healthcare workers following ENT surgical procedure in a patient at FETHA. The index case was a 15 year old boy who had local uvulectomy and later presented in FETHA, on 28th December, 2017 with fever, was unconscious and bleeding profusely from the mouth and nose. We describe the investigation of the outbreak and the epidemiological description by person, place and time characteristics of confirmed cases from January 1st – March 30th 2018.

Methods

Study area

Ebonyi State is one of the 36 states in Nigeria created in 1996. The State shares border with Benue State to the North, Enugu State to the west, Imo and Abia States to the south and Cross River State to the east. It has 13 local Government areas and an estimated population of 2.5 million.^[18] About 80% are subsistent farmers and reside in the rural areas.^[18] The patients studied were managed at the Virology centre and FETHA. The virology center is a 27 bed facility situated in FETHA The center has the isolation section for treatment of Lassa fever cases, laboratory section and dialysis section. The Federal Teaching Hospital, Abakaliki is a tertiary health care facility established in the year 2012. The hospital is a referral centre for health facilities within and outside the state and located in Abakaliki the capital of Ebonyi state Nigeria.

Case definitions

For this outbreak, we adapted and used the following case definitions:

- Suspected case of Lassa fever: Any person residing in

Ebonyi State with gradual onset fever > 380C and one or more of the following: malaise, headache, sore throat, cough, nausea, vomiting, diarrhea, myalgia, chest pain, hearing loss, bleeding (including from the mouth, nose, rectum, or vagina) from December, 28th 2017 and a history of contact with excreta of rodents or with a case of Lassa Fever without any apparent cause within three (3)

Table 1: Case fatality ratio of Lassa fever patients in Ebonyi state, Nigeria 2018.

Variables	Alive	Dead	Case fatality rate (%)
Positive cases	50	12	19
Health workers	9	4	31
Patients on Rivaberin	36	7	16

Table 2: The socio-demographic characteristics of Lassa fever patients in Ebonyi state, Nigeria, 2018.

Variable	Frequency (N)	Percent (%)
Age group		
0-9	6	9
10-19	7	11.4
20-29	11	18.2
30-39	22	36.4
40-49	8	12.5
>50	8	12.5
Sex		
Male	25	40.3
Female	37	59.7
Occupation		
Traders	16	26.23
Health workers	15	24.59
Students	11	18.03
Farmers	8	13.52
Civil servants	7	11.48
Others (traditional healers, artisans etc)	5	6.56
Level of Education		
No formal	7	4.7
Primary	13	11.7
Secondary	17	16.9
Tertiary	25	28.0

Table 3: Clinical presentation of Lassa fever cases in Ebonyi state Nigeria 2018.

Variables	Frequency (N)	Percent (%)
Fever	39	78
Headache	31	62
Cough	19	38
Vomiting	16	32
Diarrhea	16	32
Difficulty swallowing	14	28
Loss of appetite	11	22
Abdominal pain	9	18
Joint pain	9	18
Muscle pain	7	14
Nasal bleeding	7	14
Chest pain	5	10
Difficulty Breathing	5	10
Jaundice	3	6
Coma	3	6
conjunctivitis	2	4
Disoriented	1	2
Hiccup	1	2
Skin rash	1	2

weeks of the onset of illness of the earliest identified confirmed case (Technical guidelines for IDSR, Africa, 2010)

- Confirmed case of Lassa fever: A suspected case that is laboratory confirmed (positive IgM antibody, PCR or virus isolation) or epidemiologically linked to a laboratory confirmed case
- Probable: Any suspected case as defined above but who died without collection of specimen for laboratory testing.
- Contact: A person having close personal contact with the index case or a confirmed case (living with, caring for) or the laboratory staff who tests the laboratory specimens of a patient in the 3 weeks after the onset of the illness.

Sources of data

Health records review: Admission records and case notes of patients were reviewed at the FETHA and Virology centre.

Contact tracing and active case search: Data from contact tracing and active case search at FETHA, Secondary health facilities and communities in Ebonyi state were reviewed. Data on contacts were captured using the family and healthcare workers contact tracing form. Contacts were line listed and monitored daily either by visits or through phone calls. All suspected and confirmed cases of Lassa fever were line listed.

Diagnosis

Confirmation of cases was based on positive test using Lassa virus specific-specific reverse transcriptase PCR(RT-PCR) Laboratory confirmation was performed at the Institute of Lassa Fever Research and Control, Irrua Specialist Teaching Hospital,

Edo State, Nigeria and the virology centre in Abakaliki Nigeria.

Statistical analysis

Epi info software (version 7.1.4) was used for data analysis. Univariate analysis was performed for frequencies and proportions, Bivariate analysis for associations using chi square test of statistical significant. The characteristic of cases stratified by outcome variable and the presenting symptoms was presented in tables. Statistical significant level was taken at p value ≤ 0.05 at 95%confidence interval.

Ethical considerations

Ethical approval for the study was obtained from Emergency Operation Centre Ebonyi state ministry of Health . Ethical standards and best practice were adhered to throughout the conduct of the study

Results

The total number of suspected cases was 345 of which 62 cases confirmed and 12 deaths. The total case fatality rate was 19%, health workers (31%) and patients on Ribavirin (16%) [Table 1].

Table 2 shows the socio-demographic characteristics of Lassa fever patients in Ebonyi state, Nigeria 2018. The median age of confirmed cases was 35 (interquartile range of 25-43) The mean age was 35 ± 16.2 years with 36.4% within the age group 30-39 years followed by 25-29 years (18.2%) and the least 0-9 years (9%). Most were females (59.7%),traders (26.2%) and 42.9% had tertiary level of education, Table 3 shows that Fever (78%), headache (62%), cough (38%), vomiting (32%), diarrhea (32%), and difficulty swallowing (28%) were the most reported symptoms at presentation. Seven (14%) presented with nasal bleeding. Only one (7%) presented with skin rashes.

The Epidemic curve [Figure 1] shows a common source outbreak followed by a propagated pattern, The incubation period was seven days. The outbreak peak was on Epidemiological week 7 with more deaths in week 2. Having abdominal pain, not treated with rivaberin and diarrhea were related with mortality [Table 4].

Discussion

Lassa fever is endemic in Nigeria and peaks during the first 12 weeks of the year (January–March) with yearly outbreaks. In this study we present the clinical features of Lassa fever cases during 2018 outbreak in Ebonyi state. The Common presenting symptoms were fever, headache, cough and vomiting. Fever was most common but was not present in all the cases. This finding was a departure from what has been observed in earlier studies in Ebonyi state and Irua in Edo state Nigeria ^[14,19] in which fever was found in 100% of the patients. The use of antipyretics by most of the patients prior to presentation may account for the relative low prevalence of fever among our patients. Nevertheless absence of fever in a patient at presentation may not be a criterion to rule out Lassa fever.

The presenting symptoms of Fever, headache cough, nasal bleeding, and sore throat though common were not found to be significantly associated with mortality. However patients that presented with abdominal pain and/or diarrhea had low survival

Table 4: Prognostic indicators of outcome of Lassa fever cases in Ebonyi state 2018.

Variables	Clinical Alive	Outcome Dead	CI	p-value
Abdominal pain			0.022-0.500	0.0015
Yes	4	5		
No	47	6		
Diarrhea			0.030-0.521	0.0018
Yes	9	7		
No	42	4		
Ribavirin			0.817-129	0.0334
Yes	36	7		
No	1	2		

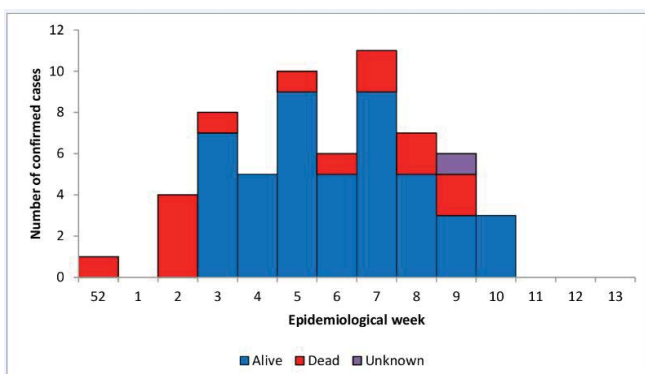


Figure 1: Epicurve of the Lassa fever outbreak in Ebonyi state, Nigeria 2018.

rate. This could be due to a possible acute kidney injury as a result of systemic immune response to infection.

The observed case fatality of 20% was lower than the findings in earlier study in Ebonyi state (30%) and lower than the findings in Edo state (24%) and much lower (68%) in Sierra Leone.^[14,19,20] It is similar to 15-20% reported in hospitalized patients.^[21] Early detection of cases by the engagement of Disease surveillance and notification officers, a functional Laboratory and prompt initiation of treatment at the virology Centre may have accounted for the low mortality. Although, there is an improved case detection and access to ribavirin some patients still presented late to the hospital. Majority of the fatalities occurred among health workers. This could be due to low index of suspicion among clinicians as Lassa fever is often considered only after patients have been treated for other ailments without improvement or died. There is need to retrain clinician on early detection and management of Lassa fever and early referral to designated treatment centre.

The age group mostly affected was 30-39 years; this is the active age group engaged in different activities-Education, business, farming, etc. This finding demonstrates the vulnerability of the young adults and the productive age group to Lassa fever infection. The finding is similar to the study by Ajayi et al. and slightly different from what was observed in Irua Edo state Nigeria.^[14,19] Majority of the patients were traders. This group of people may have been affected by eating in canteens and other unhygienic environments.

We observed an epidemiologic change in the occurrence of Lassa fever from rural to urban residents. This is similar to the finding in Jos Nigeria.^[22] Poor sanitation and over crowding predominant in most urban areas could account for this drift. It has been shown that *M. natalensis* constituted 50-60% of the rodents captured in houses but only 10-20% of those captured in surrounding agriculture and bush areas.

Conclusion

Diarrhea and abdominal pain were key symptoms related to mortality. Case fatality ratio was higher among Health worker. Even with the Ribavirin treatment, there was a high rate of fatalities underscoring the need to develop more effective treatment for Lassa fever. The engagement of Disease Surveillance Notification Officer (DSNO) in active case search and contact tracing lead to early detection and initiation of treatment.

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Conflict of Interest

The authors disclose that they have no conflicts of interest.

Authors' Contributions

Agboeze Joseph conceived and designed the study and also wrote the manuscript, Nwali igwe Matthew, Onoh Robinson, Eze Justus and Ukaegbe Emeka participated in data collection and analysis. All authors reviewed and approved the final manuscript.

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