Mortality Among Confirmed Lassa Fever Cases During the 2015–2016 Outbreak in Nigeria

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Objectives. To determine factors associated with mortality among confirmed Lassa fever cases.

Methods. We reviewed line lists and clinical records of laboratory-confirmed cases of Lassa fever during the 2016 outbreak in Nigeria to determine factors associated with mortality. We activated an incident command system to coordinate response.

Results. We documented 47 cases, 28 of whom died (case fatality rate [CFR] = 59.6%; mean age 31.4 years; SD = ±18.4 years). The youngest and the oldest were the most likely to die, with 100% mortality in those aged 5 years or younger and those aged 55 years or older. Patients who commenced ribavirin were more likely to survive (odds ratio [OR] = 0.1; 95% confidence interval [CI] = 0.03, 0.50). Fatality rates went from 100% (wave 1) through 69% (wave 2) to 31% (wave 3; χ^2 for linear trend: $P < .01$). Patients admitted to a health care center before incident command system activation were more likely to die (OR = 4.4; 95% CI = 1.1, 17.6). The only pregnant patient in the study died postpartum.

Conclusions. Effective, coordinated response reduces mortality from public health events. Attention to vulnerable groups during disasters is essential.

Public Health Implications. Activating an incident command system improves the outcome of disasters in resource-constrained settings. (*Am J Public Health.* 2018;108: 262–264. doi:10.2105/AJPH.2017.304186)

Lassa fever, a viral hemorrhagic fever, is endemic in the West African countries of Nigeria, Sierra Leone, Liberia, and Guinea, with sporadic outbreaks in other West African countries.[1] Hospitalized patients have a mortality rate of 15% to 20%, and the mortality rate can reach 50% during epidemics; 90% of women in their third trimester of pregnancy die.[2,3] The high mortality rate among those who contract Lassa fever, the challenges of containment in health care facilities, and its propensity to spread within health care settings makes it one of the diseases that health care workers dread most.[2,4] Cases are extremely difficult to differentiate clinically from other febrile illnesses in West Africa.[4,5]

Being elderly, having 1 or more comorbidities, and delay in laboratory confirmation and treatment commencement are recognized determinants of mortality.[4,6,7] The use of an incident command system (ICS) through emergency operation centers has been shown to improve coordination and overall outcomes of disasters and outbreaks, as seen in the recent West African Ebola outbreak.[8–11]

A multistate Lassa fever outbreak occurred in Nigeria between October 2015 and February 2016. We conducted a retrospective descriptive study to determine factors associated with mortality among laboratory-confirmed cases.

METHODS

Nigeria experiences sporadic outbreaks of Lassa. Most hospitals in endemic zones lack the capacity for laboratory confirmation, which results in a delay in starting treatment. Cases were geographically assigned to states with the hospitals where cases were diagnosed, even though samples were transported to few states with the capacity to conduct laboratory diagnosis. During multistate outbreaks, central coordination by the Nigeria Centre for Disease Control ensures regular communication with affected and at-risk states; this has transformed the surveillance system from passive to active, ensuring timely diagnosis and treatment commencement.

Study Design

We used line lists and clinical records to extract information on age, sex, date of onset of symptoms, date patient first went to the health facility with Lassa fever symptoms, date of sample collection, date laboratory confirmation was received, date ribavirin was commenced, comorbidities, and outcome. We defined ribavirin commencement as early if it was started within 7 days of symptom onset and as delayed if it was not. We defined suspected (patient had symptoms) and confirmed (reverse transcription polymerase chain reaction or enzyme-linked immunosorbent assay confirmed patient was infected with Lassa virus) cases on the basis of the *Technical Guidelines for Integrated Disease*

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Surveillance and Response in Nigeria.[12] We used dates of onset to develop an epi curve describing the outbreak on the basis of 3 waves. We defined a wave as the period from the beginning of a peak to the end of that peak: wave 1 was November 22, 2015, to December 6, 2015; wave 2 was December 16, 2015, to January 4, 2016; and wave 3 was January 6 to 16, 2016.

Data Analysis

We calculated age-specific case fatality rates (CFRs), odd ratios (ORs), and χ^2 for trends to compare mortality. We analyzed surveillance data collected as part of outbreak response by the Nigeria Centre for Disease Control, safeguarding the information to ensure patient confidentiality and anonymity.

RESULTS

We documented 47 confirmed cases, of whom 17 (36.2%) were females (mean age = 31.4 years; SD ±18.4 years) and 28 died (CFR = 59.7%). CFRs went from 100% (wave 1) through 69% (wave 2) down to 31% (wave 3; χ^2 for linear trend: $P < .01$; Table 1; Figure A, available as a supplement to the online version of this article at http://www.ajph.org). Overall, patients who went to a hospital or to see a doctor before we activated the ICS were more likely to die (OR = 4.4; 95% CI = 1.1, 17.6; Table A, available as a supplement to the online version of this article at http://www.ajph.org).

Our examination of the CFRs among age groups revealed that 100% of those aged 5 years or younger and those aged 55 years or older died whereas those aged 6 to 14 years survived (Table 1). Overall, those aged 30 years or older were more likely to die (OR = 4.3; 95% CI = 1.1, 16.4; Table A). Patients who live long enough to commence ribavirin are more likely to survive (OR = 0.1; 95% CI = 0.03, 0.5; Table A). The only pregnant woman in the study died postpartum.

The outbreak spread from Taraba State on November 22, 2015, to 6 additional states by January 16, 2016. Among the states studied, Taraba had the highest number of cases (n = 26) followed by Edo,[9] with CFRs of 57.7% and 77.8%, respectively. All confirmed cases reported from Lagos (n = 4), Bauchi (n = 3), and Rivers (n = 3) died. Gombe and Ekiti both had a single confirmed case who survived.

TABLE 1—Case Fatality Rates Among Confirmed Lassa Fever Cases: Nigeria, October 2015–February 2016

Characteristic	Alive, No.	Deceased, No.	CFR, %
Sex			
Male	12	18	60.0
Female	7	10	58.8
Age, y			
≤ 5	0	2	100.0
6–14	3	0	0.0
15–34	14	14	50.0
35–54	2	7	77.8
≥ 55	0	5	100.0
Time of presentation, wave			
1	0	5	100.0
2	9	20	69.0
3	9	4	30.8
Ribavirin commencement			
Not commenced	6	22	78.6
Commenced	13	6	31.6

Note. CFR = case fatality rate.

DISCUSSION

Our study shows how coordination improves timely diagnosis and treatment commencement, thereby reducing mortality. We also observed the need to pay attention to vulnerable groups, such as children aged 5 years or younger and the elderly (aged 55 years or older), during outbreaks. We found that activating the ICS provided logistic and technical support to ensure timely diagnosis, distribution of ribavirin, and guidance to health workers who performed key activities and were responsible for the observed reduction in mortality.[10] There was higher mortality among those aged 30 years or older, consistent with observations by Brosh-Nissimov, who found that being older than 18 years increased the risk of death.[7]

Lassa fever spread to states not traditionally Lassa endemic, including Lagos; this implies that, considering the 1- to 3-week incubation period, those infected with Lassa virus may travel to any part of the world through Lagos, a recognized hub for international travel. This has serious global health implications and could impede achieving the core principle and goals of the Global Health Security Agenda. The difference in mortality between those who started taking ribavirin and those who died before they had the opportunity to take ribavirin highlights the need for early diagnosis and treatment. Previous studies suggest that fear and lack of training among health care workers increase the risk of death in Lassa fever patients.[2]

The high number of cases seen in Taraba State, where the outbreak started, may reflect the poor sensitivity of the surveillance system, considering that most of the cases seen in Taraba occurred at the first stage of the outbreak by contrast with the other states, where sensitization of health care workers and public health authorities prompted the timely institution of infection prevention and control measures.

The study brings to the fore the importance of activating the ICS with a clear set of guidelines and adequate funding for managing public health emergencies. Earlier activation of the ICS might have reduced the mortality.

We did not observe a significant relationship between comorbidities and mortality, by contrast to previous studies. The poor capacity of health care facilities in resource-constrained settings to effectively diagnose and treat all underlying comorbidities may have masked this factor's contribution to mortality. We relied on self-reported information by patients or their relatives, which increased the risk of receiving inaccurate, socially acceptable responses regarding time from onset to reporting at the health facility; this limited our ability to effectively establish a clear association between delays and mortality. Furthermore, enrolling only laboratory-confirmed cases to avoid misclassification reduced the power of the study.

Effective preparedness, early detection, diagnosis, treatment, and infection prevention and control remain the cornerstone of efforts to effectively control Lassa fever outbreaks. During outbreaks, special attention should be paid to vulnerable groups, such as

children aged 5 years or younger and adults aged 55 years or older.

PUBLIC HEALTH IMPLICATIONS

Activating an ICS in functional emergency operation centers will improve the outcome of disasters in resource-constrained settings. AJPH

CONTRIBUTORS

M. I. Buba and M. M. Dalhat conceptualized and designed the study, developed and finalized the protocol, conducted the analyses, wrote the initial draft, and edited subsequent drafts of the brief. P. M. Nguku, M. S. Balogun, A. T. Bashorun, and P. Nsubuga interpreted results and edited the brief. J. O. Mohammad, I. M. Bomoi, P. Onyiah, and J. Onwujei contributed to conceptualizing the study and performed data extraction. All authors were part of the outbreak response.

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