Mortality among confirmed Lassa Fever cases in Ondo State, Nigeria, January 2017- March 2019: A cross sectional study

Olayinka S. Ilesanmi *[1,2], Oladele O. Ayodeji [3], Nelson A. Adedosu [4], Olalekan E. Ojo [5], Chukwuyem Abejegah [3], Tolulope O. Jegede [6], Tajudeen T. Adebayo [7], Isiaka A. Ayeni [8], Lanre O. Olatunde [5], Liasu A. Ahmed [9]

1. Department of Community Medicine, College of Medicine, University of Ibadan, Ibadan
2. Department of Community Medicine, University College Hospital, Ibadan
3. Department of Community Health, Federal Medical Centre, Owo
4. Department of Medical Microbiology, Federal Medical Centre, Owo
5. Department of Medicine, Federal Medical Centre, Owo
6. Department of Paediatrics, Federal Medical Centre, Owo
7. Department of Health Information Management, Federal Medical Centre, Owo
8. Department of Pharmaceutical Services, Federal Medical Centre, Owo
9. Department of Family Medicine, Federal Medical Centre, Owo

ARTICLE INFO

Original Article

Received: 14 January 2022
Accepted: 20 March 2022

OPEN ACCESS

Corresponding Author:
Olayinka Stephen Ilesanmi
drilesanmi@gmail.com

ABSTRACT

Background: Lassa fever (LF) is an acute viral haemorrhagic disease endemic in Ondo State, Nigeria. This study aimed to determine the factors associated with mortality among confirmed LF cases.

Methods: A cross sectional study design was used by conducting a retrospective review of the records of all patients who had been treated for LF at the Federal Medical Centre, Owo since 2017 till March 2019. Descriptive statistics were done, case fatality rate was calculated. Chi square tests were used to explore associations. Logistic regression was used to identify the predictors of death. Data were analysed with SPSS version 23.0. P values ≤0.05 were statistically significant.

Results: The median age was 34 years, and the inter-quartile range was 24-48 years. A total of 30 deaths (case fatality rate [CFR] = 10.9%) were recorded, of which 24 (15.5%) were males. Also, the fatality rate increased from 1.6% in 2017 to 10.5% in 2018 and 16.7% in 2019. During peak period, mortality recorded was 15(8.5%) and non-peak periods (April to December), 14(14.9%) was recorded (p=0.104). Fatality was 12.5% (1 out of 8) among pregnant women with 100% foetal death. Patients aged 18-45 years had 0.25 odds of dying (AOR = 0.25; 95%CI= 0.08, 0.76) compared to those aged ≥ 46 years. Those who commenced ribavirin ≥7 days (AOR 4.1; CI = 1.06, 15.42) and those with elevated urea level (AOR 7.5; CI = 2.5, 23.1) have more odds of dying.

Conclusions: A well-coordinated LF outbreak response is needed both at LF peak non-peak periods.

Key words: Epidemiology, Lassa Fever, Mortality, Nigeria, Surveillance

How to cite this paper:
Olayinka S. Ilesanmi, Oladele O. Ayodeji, Nelson A. Adedosu, Olalekan E. Ojo, Chukwuyem Abejegah, et al. Mortality among confirmed Lassa Fever cases in Ondo State, Nigeria, January 2017- March 2019: A cross sectional study. J Community Health Research 2022; 11(1): 5-11.

Copyright: ©2022 The Author(s); Published by Shahid Sadoughi University of Medical Sciences. This is an open-access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Introduction

Lassa fever (LF) is a viral hemorrhagic disease, with non-specific clinical manifestations that make diagnosis challenging (1). LF is characterized by body weakness, malaise, fever, vomiting, nausea, diarrhoea, cough, chest pain, muscle pain, and hearing loss (2,3). The similarity in the presentation of LF with other febrile illnesses makes LF diagnosis difficult, in fact, nearly 80% of LF cases are asymptomatic and go undiagnosed (4,5). Among LF patients who present with symptoms, clinical diagnosis of LF is made through either of the following tests: Antibody enzyme-linked immunosorbent assay (ELISA), Reverse transcriptase polymerase chain reaction (RT-PCR) assay, and antigen detection tests (6). LF is endemic in 4 countries in West Africa: Nigeria, Liberia, Sierra Leone and Guinea with sporadic cases in Mali, Burkina Faso, Benin, Togo, Ghana and Cote d'Ivoire (1). It was first discovered in Nigeria in 1969 and has continued to manifest in the country in epidemic proportions and as endemic or sporadic outbreaks (7). The disease affects about 150,000–300,000 people in West Africa yearly leading to mortality in about 5000 of these cases (8,9). In recent years, there have been yearly outbreaks with a seasonal pattern where the number of positive cases peaks from November through March (dry season) (10,11).

In 2020, the Nigeria Centre for Disease Control (NCDC) reported a total of 365 confirmed cases and 47 deaths in the first 5 weeks of the year - a case fatality rate (CFR) of 12.9% (12). Of these, Ondo, a state in the south-western region of the country has contributed the highest number of cases – 129 (35%) with a CFR of about 13% (13). Ondo state is endemic for LF, accounting for 35-50% of total number of cases in Nigeria since 2017. In view of this, a LF Infection Control and Research Centre (ICRC) was started at Federal Medical Centre, Owo, Ondo State in 2017. This centre is dedicated to the management of LF patients.

Other risk factors for mortality have been identified by some studies in other centres in the country. These determinants of mortality include extremes of age, pregnancy status in women, acute kidney injury, "creatinine and urea levels", delay in treatment commencement as well as delay in the activation of the incident command system (14,15). It is pertinent to examine the contributory factors to LF-related mortality in Ondo State, Nigeria. This study therefore aimed to determine mortality related factors among confirmed LF cases at the LF Infection Control and Research Centre, Federal Medical Centre, Owo, Ondo State.

Methods

Study Area

This study was done at the Federal Medical Centre located in Owo, Ondo State Nigeria, a tertiary health facility established to serve the specialized health needs of Owo, Akure and their environs. The diagnosis of LF was confirmed by Polymerase Chain Reaction test. All LF positive patients seen at the FMC Owo were referred for treatment prior to January 2017. The Infection Control and Research Centre (ICRC) at the Federal Medical Centre started as Infection Control Ward (ICW) in January 2017 in response to managing LF. The ICW was renamed ICRC after the unprecedented outbreak of LF disease in the first few months of 2018. A-34-bedded facility was provided on the 28th day of February 2018. The ICRC collaborates with other national and international organizations for research and management including Nigeria Centre for Disease Control (NCDC), Alliance for International Medical Action (ALIMA) and African Centre of Excellence for Genomics of Infectious Diseases (ACEGID).

The activities of the ICRC are controlled through an Emergency Operations Centre (EOC) that was set up to serves as the command centre for all activities during an outbreak. The various pillars of the EOC form the foundation on which the EOC functions. In this current outbreak, the National LF EOC operates on six major pillars as activated by the Nigeria Centre for Disease Control: Coordination, Surveillance/Epidemiology; Case management; Infection Prevention and

Control/Safe Burial; Risk Communication; Logistics; and supplies and Laboratory. Response activities revolve around these pillars.

Study Design

A cross sectional study design was used by conducting a retrospective review of the records of all patients who had been treated for LF at the facility since 2017 till March 2019.

Sampling technique

All the records of patients who had been treated at the facility since 2017 till March 2019 were included. Line lists and clinical records were used to extract information on age, sex, date of onset of symptoms, date of first presentation at the health facility with LF symptoms, date of sample collection, date laboratory confirmation was received, date ribavirin was commenced, comorbidities, and outcome.

Data analysis

We analysed surveillance, epidemiological, clinical and laboratory data during the 2017 to 2018 outbreak and the peak period (January to March) of 2019. Descriptive statistics were done, case fatality rate (number of death/ those at risk of dying * 100) was calculated. Associations between independent variables and death were explored with Chi square tests. Logistic regression was used to identify the predictors of death. Normal creatinine level was defined as 0.6 to 1.2 milligrams (mg) per decilitre (dL) in adult males and 0.5 to 1.1 milligrams per decilitre in adult females. Creatinine levels were measured by the Jaffe method, which is an alkaline-based method. Creatinine in the sample reacts at an alkaline PH with the picrate to constitute a creatinine-picrate complex. We defined ribavirin commencement as early if it was initiated within 7 days of symptom onset and as delayed if it was not. Peak transmission period is the first 12 weeks (January-March) yearly. We defined confirmed cases based on the Technical Guidelines for Integrated Disease Surveillance and Response in Nigeria (16,17). Data was analysed with Statistical Package for the Social Sciences version 23.0. P values ≤0.05 were statistically significant.

Results

Out of the 440 patients tested, 308(70%) were positive for LF. However, records were available for review for only 276 of these positive cases. The median age was 34 years (inter quartile range= 24-48 years). Among those aged 46 years and above, 16(20%) died compared to 3(10.7%) among patients less than 18 years (p=0.006). Death among males was 24(15.5%), while death among females was 6(5%), (p=0.005). In patients with elevated creatinine level, 15(24.2%) died compared to 6(4.1%) of those with normal creatinine level (p<0.001). There was no difference in death rate between the peak and non-peak period. In all 30 patients died (case fatality rate [CFR] = 10.9%; Fatality rates went from 1.6% in 2017 to 10.5% in 2018 and 16.7% in 2019, p=0.025. Figure 1. Fatality was 12.5% (1 out of 8) among pregnant women with 100% foetal death. CFR was 16.3% among those who commenced Ribavirin 7 days or more after onset of symptoms later from onset, 24.2% in those with elevated creatinine and 40.7% in those with elevated urea. Table 1

The leading signs and symptoms that LF confirmed patients presented with were fever (251), body weakness (145) and headache (100).

Table 2 shows the predictors of death among confirmed LF cases January 2017– March 2019, Ondo State, Nigeria. Patients who were more likely to die were, those commenced on Ribavirin on or after the 7th day of symptoms onset (Adjusted odds ratio [ORadj] for age group, sex, commencement of ribavirin, and urea level which were significant at the bivariate level. Those who commenced ribavirin on or after the seventh day of symptoms onset had 4 times odds of dying (ORadj = 4; 95% confidence interval [CI] = 1.1, 15.4), those with elevated urea level had eight times odds of dying (ORadj 7.5; CI = 2.5, 23.1), While patients aged 18-45 years had 75% lesser odds of dying (ORadj = 0.25; CI= 0.08, 0.76) after adjusting for other variables.

Table 1. Factors associated with death among confirmed Lassa Fever cases January 2017– March 2019, Ondo State, Nigeria

Variable	Died n (%)	Alive n (%)	Case Fatality Rate %	X^2	P-value
Age group (years)					
<18	3(10.7)	25 (89.3)	10.7	10.12	0.006
18-45	11 (6.5)	157 (93.5)	6.5		
≥46	16 (20)	64 (80)	20		
Sex					
Male	24 (15.5)	131 (84.5)	15.5	7.77	0.005
Female	6 (5)	115 (95)	5		
Commencement of Ribavirin					
<7 days	8(5.7)	133(94.3)	5.7	8.03	0.005
≥7 days	22(16.3)	113(83.7)	16.3		
Creatinine level					
Elevated	15 (24.2)	47 (75.8)	24.2	19.16	<0.001
Normal	6 (4.1)	139 (95.9)	4.1		
Urea level					
> 20 mg/dL	11 (40.7)	16 (59.3)	40.7	31.89	<0.001
≤ 20 mg/dL	10 (5.6)	170 (94.4)	5.6		
Seasonality					
January - March (Surge period)	15 (8.5)	162 (91.5)	8.5	2.647	0.104
April-December	14 (14.9)	80 (85.1)	14.9		

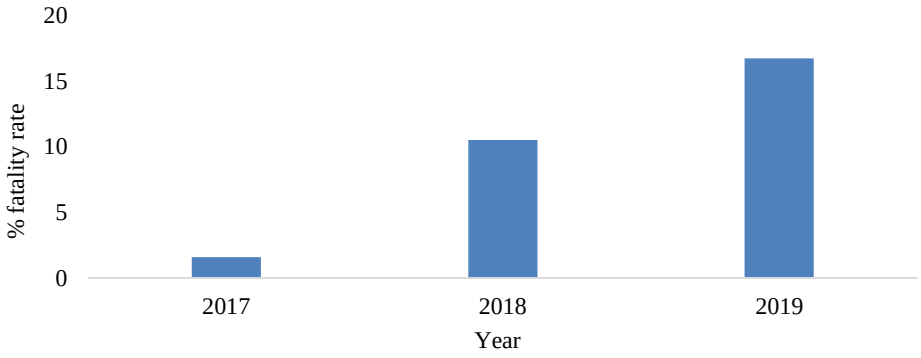

Figure 1. Case fatality rates of Lassa Fever, Federal Medical Centre, Owo, Ondo State, Nigeria, January 2017 to March 2019

Table 2. Predictors of death among confirmed Lassa Fever cases January 2017– March 2019, Ondo State, Nigeria

Characteristics	AOR	95% CI of OR Lower	95% CI of OR Upper	p-value
Age group				
<18	0.25	0.03	2.48	0.24
18-45	0.25	0.08	0.76	0.014
≥46	1			
Sex				
Male	2.9	0.89	9.2	0.08
Female	1			
Commencement of Ribavirin				
<7 days	1			
≥7 days	4.1	1.06	15.42	0.04
Urea level				
Abnormal	7.5	2.47	23.08	<0.001
Normal	1			

Discussion

Our study was conducted at the FMC, Owo in Ondo State, Nigeria, a facility with an activated LF EOC. We reviewed the records of confirmed LF cases from January 2017 to March 2019. The CFR of the reviewed cases was 10.9%. This was lower than the national rates: the 2020 cumulative (week 1-7) CFR was 17.6% and 21.1% for the same period in year 2019 (17). The CFR in this study was 20% among those aged 46 years and above. This is like previous studies that reported high CFRs among the elderly (7,18). The similarity of our findings with the reference literature agrees with the knowledge that advancements in age are associated with increased susceptibility to infections due to a waning of the immune system at such period.

We also found that fatality among infected pregnant women was 12.5%. The case fatality found out in this study contradicts the CF obtained in studies conducted among the general population in Nigeria during the 2016 LF outbreak. Buba et al. reported a CF of 59.6%, while Shehu et al. stated a CF of 36%, and corroborated by other studies (7,9,10). The disparity of our findings from these literatures could be explained by the early presentation of pregnant women at health facilities. The enrolment of pregnant women on weekly antenatal clinics could help identify suspected cases of LF early enough for commencement of treatment.

The study also showed that age, sex, period of commencement of ribavirin, creatinine and urea levels were significantly associated with mortality. The regression analysis showed that, unlike sex, the age, period of commencement of ribavirin and urea level were important predictors of death among LF cases. This has been alluded to by findings of other studies that the extremes of ages are strong predictors of dying from LF (14). Patients who were 45 years or less in our study had about 75% odds of surviving the condition. This is very close to the higher CFR found in patients that were 50 years and above in a study that examined the clinical and laboratory predictors of LF outcome in a dedicated treatment facility in Nigeria (12). This is however, slightly different from the finding of a study that assessed the mortality among confirmed LF cases during the 2015-2016 outbreak in Nigeria (8). The differences in these studies could be due to the differences in the periods within which both studies were conducted. Our study also reported higher mortality among patients who were relatively younger (30 years and older).

Our study again showed that the commencement of ribavirin early in the management of cases can reduce mortality from LF. Persons that had ribavirin instituted in their management after seven days of developing symptoms were four times more likely to die from LF compared to those that had it introduced earlier. This agrees with findings from previous studies (12, 17). The absence of costs attached to LF treatments should be widely communicated through public health campaigns. LF awareness campaigns should not just be limited to free treatment availability but should also encompass the risk factors for LF as well as the modes of transmission (19, 20). This is likely to improve the chances of enrolment for LF-infected persons who may be dissuaded from seeking care due to the perceived cost of care. Furthermore, patients with abnormal urea level were almost eight times more likely to die from LF when compared with those with no apparently impaired blood urea. Acute kidney injury due to the direct effects of the virus on the kidney has though been strongly linked to death among LF positive (8). Kidney injury is associated with death among LF positive patients. LF positive patients with signs of renal compromise should have appropriate interventions incorporated early into their management to prevent adverse outcome.

Strengths

This study successfully identified that the LF outbreak occurs all-round the year. In spite of the huge contributions of the NCDC during the dry season, a response which ends annually in March, the need for sustained outbreak response in non-peak period was highlighted in this study.

Limitations

There are two limitations inherent in this study. The use of secondary data could have limited our findings. Also, the incompleteness of data in some areas for confirmed cases may have limited the findings. These limitations, however, do not question the credibility of the findings in this study. Future prospective research is required regarding the events of mortality among LF confirmed persons.

Conclusion

LF fatality increased between 2017 and 2019. More fatality occurred in males, and the predictors of death were older age, late commencement of treatment. Coordinated response is important during both peak and non-peak period to prepare adequately for subsequent outbreaks and to enable timely response. In addition, the national guidelines on the clinical management of LF should be strictly adhered to. Early presentation and high index of suspicion among health workers are possible factors that will aid prompt diagnosis, hence the need for early commencement of treatment.

Acknowledgements

The authors are grateful to the Research Assistants who actively participated in the data extraction activity. Ethical approval was obtained from the Health Research Ethics Committee of FMC, Owo on 1st March, 2019 (FMC/OW/380/VOL. LXVII/187).

Conflict of interests

The authors declare no competing interest. No external funding was received for this study. The authors take complete responsibility for the integrity and accuracy of the data.

Authors' contributions

O.S.I., O.O.A. and C.A designed the study; O.S.I, O.O.A., N.A.A., O.E.O. T.O.J., T.T.A. and I.A.A. contributed to data collection; O.S.I., analysed the data and wrote the initial draft of the manuscript, all authors contributed to writing, editing, reviewing the manuscript for important intellectual content.

References

1. Salami K, Gsell PS, Olayinka A, et al. Meeting report: WHO consultation on accelerating Lassa fever vaccine development in endemic countries. Vaccine. 2020;38(26):4135-4141.
2. Ijarotimi IT, Ilesanmi OS, Aderinwale A, et al. Knowledge of Lassa fever and use of infection prevention and control facilities among health care workers during Lassa fever outbreak in Ondo State, Nigeria. Pan African Medical Journal. 2018; 30: 56.
3. McCormick JB. Lassa fever. In: Saluzzo JF, Dodet B, editors. Emergence and Control of Rodent-borne Viral Diseases. Paris: Elsevier; 1999. pp. 177–795.
4. Kennlyside RA, McCormick JB, Webb PA, et al. Case-control study of Mastomys natalensis and humans in Lassa virus-infected households in Sierra Leone. American Journal of Tropical Medicine and Hygiene. 1983;32(4):829–37.
5. Ajayi NA, Nwigwe CG, Azuogu BN, et al. Containing a Lassa fever epidemic in a resource-limited setting: outbreak description and lessons learned from Abakaliki, Nigeria (January-March 2012. International Journal of Infectious Diseases. 2013; 17(11):e1011–6.
6. World Health Organization. Lassa fever. Available from: https://www.who.int/news-room/fact-sheets/detail/lassa-fever. Accessed 20 November 2020.
7. Akpede GO, Asogun DA, Okogbenin SA, et al. Lassa fever outbreaks in Nigeria. Expert Review of Anti-Infective Therapy. 2018;16(9):663–666.
8. Olayemi A, Cadar D, Magassouba N, et al. New Hosts of The Lassa Virus. Scientific Reports.2016;3-6.
9. Buba MI, Dalhat MM, Nguku PM, et al. Mortality Among Confirmed Lassa Fever Cases During the 2015–2016 Outbreak in Nigeria. American Journal of Public Health.2018;108(2):262–4.
10. Shehu NY, Gomeri P, Isa SE, et al. Lassa fever 2016 outbreak in Plateau State, Nigeria – The changing epidemiology and clinical presentation. Frontiers in Public Health. 2018;6:232. doi: 10.3389/fpubh.2018.00232

11. Mofolorunsho KC. Outbreak of lassa fever in nigeria: Measures for prevention and control. Pan Africa Medical Journal. 2016; 23: 210.
12. Asogun DA, Adomeh DI, Ehimuan J, et al. Molecular Diagnostics for Lassa Fever at Irrua Specialist Teaching Hospital, Nigeria: Lessons Learnt from Two Years of Laboratory Operation. PLoS Neglected Tropical Diseases. 2012;6 (9):e1839
13. NCDC 2020. An update of Lassa fever outbreak in Nigeria. Available at: https://ncdc.gov.ng/diseases/sitreps/%3fcat%3d5%26name%3dAn+update+of+Lassa+fever+outbreak+in+Nigeria. Accessed September 26 2020.
14. Okokhere P, Colubri A, Azubike C, et al. Clinical and laboratory predictors of Lassa fever outcome in a dedicated treatment facility in Nigeria: an observational cohort study HHS Public Access. Lancet Infectious Diseases. 2018; 18(6):684–695.
15. Ilori EA, Furuse Y, Ipadeola OB, , et al. Epidemiologic and Clinical Features of Lassa Fever Outbreak in Nigeria, January 1–May 6, 2018. Emerging Infectious Diseases. 2019; 25(6):1066-1074.
16. NCDC, 2020. Technical guidelines for integrated disease surveillance and response in Nigeria. Available at: http://www.ncdc.gov.ng/ themes/common/docs/protocols/4_1476085948.pdf. Accessed September 26, 2020.
17. NCDC, 2020. Lassa fever Situation Report: 2020 Week 7. 2020.Available at: https://www.ncdc.gov.ng/themes/commonfiles/sitreps/6972c8ce98679587edf51016e9ab4051.pdf. Accessed September 26, 2020.
18. Ehichioya, DU, Hass M, Becker-Ziajar B, et al. Current molecular epidemiology of Lassa virus in Nigeria. Journal of Clinical Microbiology. 2011; 49: 1157–1161
19. Akpede GO, Asogun DA, Okogbenin SA, et al. Caseload and Case Fatality of Lassa Fever in Nigeria, 2001–2018: A Specialist Center's Experience and Its Implications. Frontiers in Public Health. 2019; 25.
20. Asogun D, Okokhere PO, Okogbenin S,. Lassa fever awareness and practices in a Nigerian rural community. International Journal of Infectious Diseases. 2010; 14(1). e20