

Review Article

Mortality Among Lassa Fever Patients: A Systematic Review

Peter Ekpunobi Chime^{1, *}, Ethel Nkechi Chime^{2, 3}, Uzoma Chukwunonso Okechukwu¹

¹Department of Medicine, Enugu State University of Science and Technology Teaching Hospital, Enugu, Nigeria

²Department of Otorhinolaryngology, University of Nigeria Teaching Hospital, Enugu, Nigeria

³Department of Otorhinolaryngology, Enugu State University of Science and Technology Teaching Hospital, Enugu, Nigeria

Email address:

pe4chyme@yahoo.com (P. E. Chime), ethel.chime@unn.edu.ng (E. N. Chime), uzoweb@yahoo.com (U. C. Okechukwu)

*Corresponding author

To cite this article:

Peter Ekpunobi Chime, Ethel Nkechi Chime, Uzoma Chukwunonso Okechukwu. Mortality Among Lassa Fever Patients: A Systematic Review. *American Journal of Internal Medicine*. Vol. 9, No. 2, 2021, pp. 87-90. doi: 10.11648/j.ajim.20210902.15

Received: February 24, 2021; **Accepted:** March 8, 2021; **Published:** March 26, 2021

Abstract: Background: Lassa fever is a disease of public health importance because of its morbidity and associated mortality and also because of its potential for residual morbidity such as hearing loss and social stigma. Knowledge of the mortality among Lassa fever patients is one way of assessing the effectiveness of the current strategies employed in Lassa fever management. This article is aimed at reviewing mortalities among Lassa fever patients. Methods: The relevant articles for the review were searched and obtained through the PubMed database. Data of interest were confirmed cases of Lassa fever, number of deaths and case fatality rates. Findings: All the studies reviewed were carried out in the Lassa fever endemic zone of West Africa. The case fatality rates in Lassa fever ranged from 24% to 61%, with a mean of 36%. More cases of Lassa fever and more deaths occurred during Lassa fever outbreaks. Patient's age, co-existing medical conditions as well as complications arising from Lassa virus infection were the determinant factors for patients' survival. Conclusion: The case fatality rate in Lassa fever was very high among hospitalized patients. Timely therapeutic intervention, infection prevention and control measures and well-coordinated response during Lassa fever outbreaks are necessary for favourable outcomes in Lassa fever management.

Keywords: Death in Lassa Fever, Case Fatality in Lassa Fever, Patient's Survival in Lassa Fever

1. Introduction

Lassa fever is a viral haemorrhagic fever endemic in West African countries [1]. Most cases of Lassa virus infection present with mild or no symptoms. In those with symptoms, the incubation period is variable. The symptoms are nonspecific, the commonest symptom being fever [2]. Other symptoms include headache, cough, sore throat, diarrhea and vomiting [2, 3]. Bleeding can occur from any part of the body including the eyes (conjunctival erythema, subconjunctival hemorrhage) [4], ears, nose and mouth [5]. Bleeding in Lassa fever can be subtle [6]. Shock and multi organ failure may be the terminal events in those who succumb to the illness.

The mortality rate in Lassa virus infection is low (about 1% [1, 3]) in the general population because in many cases Lassa

virus infection is asymptomatic [3]. In their study in Guinea, Kernéis et al [7] found Lassa fever seroprevalence of 12.9% and 10.0% in village and urban participants respectively, suggesting prior exposure to Lassa virus. Among those with positive serology, 13% of them had no clinical signs in the previous twelve months, which is a corroborative evidence that Lassa virus infection can be asymptomatic.

However, among hospitalized patients, the case fatality rates in Lassa fever are high [8-10]. Lassa fever is of public health importance because of its high mortality among hospitalized patients, and also because of its potential for residual morbidity such as hearing loss [11, 12] and social stigma. Knowledge of the mortality among Lassa fever patients is one way of assessing the effectiveness of the current strategies employed in Lassa fever management.

This article is aimed at reviewing mortalities among Lassa

fever patients.

2. Methods

The relevant articles for the review were searched through the PubMed database using the term “Lassa fever,” “case fatality rate,” and “mortality in Lassa fever.” The inclusion criteria were studies published in English with no restrictions in terms of age or gender. The relevant articles were obtained. Data of interest were confirmed cases of Lassa fever, number of deaths and case fatality rates.

3. Findings

3.1. Case Fatality Rates in Lassa Fever

Nine studies involving a total of 686 confirmed cases of Lassa fever and also involving children and adults were included in the review. There were varying rates of case fatality [2, 8-10, 13-17].

A retrospective study on 60 suspected cases of Lassa fever in Edo state of Nigeria was done in which 25 of them were confirmed to have Lassa fever. Twenty-nine percent (29%) of the 25 patients died [2].

In a study on the epidemiology of Lassa fever and factors associated with Lassa fever deaths in Nigeria, from January 2015 to December 2018. There were 76 confirmed cases of Lassa fever out of which 54% of them died. The authors reported an increase in the incidence of Lassa fever as well as in the case fatality rate between 2015 and 2018 [8].

Another study on mortality among Lassa fever patients during the 2015 to 2016 outbreak in Nigeria attempted to determine the factors associated with mortality. There were 47 confirmed cases of Lassa fever out of which 28 (59.6%) died [9].

A retrospective study in a rural district hospital in Sierra Leone involved all children and women with obstetric emergencies in the hospital with either suspected or confirmed Lassa fever between April 2011 and February 2012 [10]. There were 84 suspected cases consisting of 73 children and 10 pregnant women. The only man among them was a member of the hospital staff. In all there were 36 confirmed cases and 22 (61%) of them or died. The high case fatality rate was partly explained by the fact that the hospital was a referral facility for children and pregnant women to which patients with severe illness were likely to present [10]. It is also known that pregnancy is one of the factors that predispose patients to unfavourable treatment outcome in Lassa fever [18].

A retrospective study done in a dedicated hospital in Nigeria on 291 consecutive confirmed cases of Lassa fever patients between 2011 and 2015, had only 284 patients with known outcomes. Sixty-eight (24%) of the 284 patients died [13].

Another large retrospective study in Nigeria involved 1,650 patients that presented between 2009 and 2010. Out of the 1,650 patients, 198 patients tested positive for Lassa virus. Out of the 198 patients, 109 survived, 61 died and the outcome was

unknown in remaining 28 of the patients. The percentage death was 36% in the 170 patients with known outcomes [14].

In a study in North-Central Nigeria by Shehu *et al* [15], there were 34 suspected cases of Lassa fever out of which there were eleven confirmed cases. For the eleven confirmed cases, the percentage death was 36%.

In a study in South-East Nigeria on Lassa fever outbreak that occurred between January and March 2012 in Abakaliki, Nigeria, there were 20 suspected cases of Lassa fever out of which 10 cases were confirmed. Forty percent of the 10 confirmed cases died [16].

Yadouleton *et al* [17] reported on the Lassa fever outbreak in in Benin Republic between 2014 and 2016. There were two confirmed cases of Lassa fever in 2014 and 18 confirmed cases in 2016, making it a total of 20 cases. The percentage of patients that died was 50%. There were also probable cases and suspected cases which were not included in this analysis.

A pooled analysis of the nine studies in this review revealed a total of 686 confirmed cases of Lassa fever of which the outcomes were known and a total of 247 deaths, giving a case fatality rate of 36%.

3.2. Seasonal Changes in Lassa Fever Incidence and Associated Deaths

In West Africa, Lassa fever is endemic and outbreaks usually occur during the dry season. Thus, the incidence of Lassa fever is higher during the dry season and less during the wet season [14, 18]. However, in post-conflict Sierra Leone, a second peak was observed during the rainy season which was attributed to the effect of movement of people during the civil war [18].

Increase in the incidence of Lassa fever, as well as in the number of deaths was reported between 2016 and 2020 [19]. However, in terms of case fatality rates during this period, the case fatality rate was highest in 2017 (26.5%) when compared to 2018 (23.7%), 2019 (19.6%) and 2020 (13.4%) [19].

3.3. Predictors of Mortality in Lassa Fever

Delay in seeking medical care had unfavourable effects on patients' survival [8, 10, 14]. Studies have shown the efficacy of Ribavirin in Lassa fever especially if given early in the course of the disease [10, 18].

Gender and occupation appeared to have no significant effect on patients' survival [13].

Age was an important determinant of patients' survival in Lassa fever. Lassa fever associated mortality increases with increasing age [13]. Although, some studies reported a higher mortality among older patients, Buba *et al* reported a higher mortality among younger and older patients [9].

High creatinine levels, high blood urea levels and serum potassium [13, 14] which are markers of renal injury are important predictors of treatment outcome. Aspartate aminotransferase level which is a marker of hepatic involvement is another laboratory predictor of treatment outcome [13].

Co-existing medical conditions such as pregnancy is a

significant predictor of treatment outcome in Lassa fever [10]. Pregnant females with Lassa fever fare poorly [18, 21]. Foetal outcome is also adversely affected in Lassa fever [18, 21]. There is a high incidence of acute kidney injury (28%) in Lassa fever and it is a predictor of poor treatment outcome in Lassa fever [13].

A well-coordinated response during Lassa fever outbreak and institution of infection prevention and control measures helped in reducing Lassa fever associated morbidity and mortality [9].

3.4. Mortality Among Healthcare Workers

During the Nigerian Lassa fever outbreak of January to May 2018, 37 healthcare workers were infected in which there were 8 deaths giving a case fatality rate of 21.6% [20]. In their study in Sierra Leone, Fraser *et al* [22] found a significant number of hospital workers to be seropositive for Lassa fever in a sero-prevalence study. However, it was not known whether the Lassa virus infection was nosocomially acquired or not.

4. Conclusion

In the Lassa fever endemic zone of West Africa, case fatality rates were high among hospitalized Lassa fever patients. The case fatality rates ranged from 24% to 61% with a mean of 36%. Among the nine studies reviewed, there was a total of 686 confirmed cases of Lassa fever with known outcomes and a total of 247 deaths.

There has been increasing incidence of Lassa fever, as well as number of deaths in Lassa fever. More cases of Lassa fever and more deaths from Lassa fever occur during Lassa fever outbreaks which are usually during the dry season.

Management outcome in Lassa fever depends on the patient's age, co-existing medical conditions such as pregnancy as well as the degree of complications resulting from Lassa fever, and the promptness of a well-coordinated response and institution of infection prevention and control measures.

References

- [1] World Health Organization. Lassa fever Fact sheet 2017. <http://www.who.int/mediacentre/factsheets/fs179/en/> [Accessed 2 January, 2021].
- [2] Ehichioya, D. U., Asogun, D. A., Ehimuan, J., Okokhere, P. O., Pahlmann, M., *et al* (2012) Hospital-based surveillance for Lassa fever in Edo State, Nigeria, 2005-2008. *Trop Med Int Health*, 17 (8), 1001-4.
- [3] Centers for Disease Control and Prevention. Lassa fever. <https://www.cdc.gov/vhf/lassa/transmission/index.html> [Accessed 2 January, 2021].
- [4] Kofman, A., Choi, M. J., Rollin, P. E. (2019) Lassa fever in Travelers from West Africa, 1969 - 2016. *Emerg Infect Dis.* 25 (2), 236-239.
- [5] Dzotsi, E. K., Ohene, S. A., Asiedu-Bekoe, F., Amankwa, J., Sarkodie, B. *et al.* (2012) The first cases of Lassa fever in Ghana. *Ghana Med J.* 46 (3), 166-70.
- [6] Chime, P. E., Chime, E. N., Ndiabuagu, E., Ekochin, F. C., Arinze-Onyia, S. and Oti, B. (2020) Lassa fever Case Report: Challenges in Making Early Diagnosis. *Advances in Infectious Diseases*, 10, 228-234.
- [7] Kernéis, S., Koivogui, L., Magassouba, N. *et al.* (2009) Prevalence and risk factors of Lassa seropositivity in inhabitants of the forest region of Guinea: a cross-sectional study. *PLoS Negl Trop Dis.* 2009; 3 (11): e548. (Published correction appears in *PLoS Negl Trop Dis.* 2010; 4 (1)).
- [8] Abdulkarim, M. A., Babale, S. M., Umeokonkwo, C. D., Bamgboye, E. A., Bashorun, A. T. *et al.* (2020) Epidemiology of Lassa fever and Factors Associated with Deaths, Bauchi State, Nigeria, 2015 - 2018. *Emerg Infect Dis.* 26 (4), 799-801.
- [9] Buba, M. I., Dalhat, M. M., Nguku, P. M., Waziri, N., Mohammad, J. O. *et al.* (2018) Mortality among confirmed Lassa fever cases during the 2015-2016 outbreak in Nigeria. *Am J Public Health*, 108, 262-264.
- [10] Dahmane, A., Van Griensven, J., Van Herp, M., Van den Bergh, R., Nzomukunda, Y. *et al.* (2014) Constraints in the diagnosis and treatment of Lassa fever and the effect on mortality in hospitalized children and women with obstetric conditions in a rural district hospital in Sierra Leone. *Trans R Soc Trop Med Hyg.* 108, 126-3227.
- [11] Richmond, J. K. and Baglole, D. J. (2003) Lassa fever: Epidemiology, Clinical Features, and Social Consequences *BMJ*, 327, 1271-1275.
- [12] Okokhere, P. O., Ibekwe, T. S., Akpede, G. O. (2009) Sensorineural hearing loss in Lassa fever: two case reports. *J Med Case Rep*, 3: 36.
- [13] Okokhere, P., Colubri, A., Azubike, C. *et al.* (2018) Clinical and laboratory predictors of Lassa fever outcome in a dedicated treatment facility in Nigeria: a retrospective, observational cohort study. *Lancet Infect Dis.*, 18 (6), 684-695.
- [14] Asogun, D. A., Adomeh, D. I., Ehimuan, J., *et al.* (2012) Molecular diagnostics for Lassa fever at Irrua specialist teaching hospital, Nigeria: lessons learnt from two years of laboratory operation. *PLoS Negl Trop Dis.*; 6 (9): e1839. doi: 10.1371/journal.pntd.0001839. Accessed 15/02/2021.
- [15] Shehu, N. Y., Gomerep, S. S., Isa, S. E., Iraoyah KO, Mafuka J *et al.* (2018) Lassa fever 2016 Outbreak in Plateau State, Nigeria - The Changing Epidemiology and Clinical Presentation. *Front. Public Health*, <https://doi.org/10.3389/fpubh.2018.00232>.
- [16] Ajayi, N. A., Nwigwe, C. G., Azuogu, B. N., Onyire, B. N., Nwonwu, E. U. *et al.* (2013) Containing a Lassa fever epidemic in a resource-limited setting: outbreak description and lessons learned from Abakaliki, Nigeria (January - March 2012). *Int J Infect Dis.* 2013; 17: e1011-6.
- [17] Yadouleton, A., Picard, C., Rieger, T., Loko, F., Cadar, D., Kouthon, E. C., Job, E. O. (2020) Lassa fever in Benin: description of the 2014 and 2016 epidemics and genetic characterization of a new Lassa virus. *Emerg Microbes Infect.* 9 (1), 1761-1770.

- [18] Shaffer JG, Grant DS, Schieffelin JS, Boisen ML, Goba A, Hartnett JN, et al. (2014) Lassa fever in Post-Conflict Sierra Leone. *PLoS Negl Trop Dis* 8 (3): e2748. <https://doi.org/10.1371/journal.pntd.0002748> Accessed 15/02/2021.
- [19] Yaro, C. A., Kogi, E., Opara, K. N. *et al.* Infection pattern, case fatality rate and spread of Lassa virus in Nigeria. *BMC Infect Dis* 21, 149 (2021). <https://doi.org/10.1186/s12879-021-05837-x> Accessed 15/02/2021.
- [20] Ilori EA, Furuse Y, Ipadeola OB, Dan-Nwafor CC, Abubakar A, Womi-Eteng OE, Ogbaini-Emovon E et al. Nigeria Lassa fever National Response Team. Epidemiologic and Clinical Features of Lassa fever Outbreak in Nigeria, January 1-May 6, 2018. *Emerg Infect Dis*. 2019 Jun; 25 (6): 1066-1074.
- [21] Price ME, Fisher-Hoch SP, Craven RB, McCormick JB. A prospective study of maternal and fetal outcome in acute Lassa fever infection during pregnancy. *BMJ*. 1988; 297 (6648): 584-7.
- [22] Fraser DW, Campbell CC, Monath TP, Goff PA, Gregg MB. Lassa fever in the Eastern Province of Sierra Leone, 1970-1972. I. Epidemiologic studies. *Am J Trop Med Hyg*. 1974 Nov; 23 (6): 1131-9.