

Hearing Loss in Lassa Fever: A Systematic Review

Ethel Nkechi Chime^{1,2*}, Peter Ekpunobi Chime³, Jones Ndubuisi Nwosu¹

¹Department of Otorhinolaryngology, University of Nigeria Teaching Hospital, Ituku-Ozalla, Nigeria

²Department of Otorhinolaryngology, Enugu State University of Science and Technology Teaching Hospital, Parklane, Nigeria

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

Email: *ethel.chime@unn.edu.ng, pe4chyme@yahoo.com, jones.nwosu@unn.edu.ng

How to cite this paper: Chime, E.N., Chime, P.E. and Nwosu, J.N. (2022) Hearing Loss in Lassa Fever: A Systematic Review. *Open Journal of Preventive Medicine*, 12, 239-247.
<https://doi.org/10.4236/ojpm.2022.1211018>

Received: August 28, 2022

Accepted: November 11, 2022

Published: November 14, 2022

Copyright © 2022 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Background: Lassa fever is a viral haemorrhagic fever associated with several complications which include hearing loss. Hearing loss in Lassa fever may become residual with its negative impact on the quality of life. **Purpose:** This paper is a review of various studies on Lassa fever related hearing loss. **Methods:** Systematic literature review was done on articles on Lassa fever patients and Lassa fever survivors. Relevant articles published in English between 1969 and 2021 were searched for using Google Scholar and PubMed databases. Eight studies which met the inclusion criteria were finally selected and included in the review. The variables of interest were extracted from the full-text articles. **Results:** Lassa fever related hearing loss occurs in both sexes and in all age groups. The incidence of self-reported hearing loss ranged from 12.5% to 30% with a mean of 17.6%. The incidence of audiometrically determined sensorineural hearing loss ranged from 13.5% to 29% with a mean of 22.1%. Hearing loss persisted in 64% of those that were followed up. Cases of hearing loss varied in severity, ranging from mild to profound. No successful specific treatment for Lassa fever related hearing loss was reported apart from hearing rehabilitation. **Conclusion:** Hearing loss among Lassa fever patients remains a major challenge. Lack of effective treatment for Lassa fever related hearing loss is a serious gap in the management of Lassa fever patients which should be addressed in future research.

Keywords

Hearing Loss, Hearing Impairment, Lassa Fever

1. Introduction

Lassa fever is a viral haemorrhagic fever, first discovered in Nigeria in 1969 [1].

Lassa fever is caused by Lassa virus which is an arenavirus [2]. Lassa virus is a single-stranded RNA virus.

Lassa virus infection can be contracted directly from infected multimammate rat (*Mastomys natalensis*) or from food contaminated by the urine or excreta of infected *Mastomys natalensis*. Lassa virus can also be contracted from the body fluid of a person infected with Lassa virus [3]. The presenting symptoms and signs in Lassa fever include fever, headache, general body weakness, sore throat, cough, joint or body pain, abdominal pain, vomiting, diarrhea and hearing loss [3]-[9]. In severe cases, hypotension, bleeding, encephalitis, acute respiratory distress, acute kidney injury or multiple organ failure can occur. Hearing loss is the most common residual complication in those that survive Lassa virus infection.

The first description of hearing loss in Lassa fever was by White in 1972, when he reported hearing loss in four out of 22 Lassa fever patients treated in Northern Nigeria between in 1970 [10]. Subsequently, other researchers have reported hearing loss among Lassa fever patients [11]-[16]. Mertens *et al.* reported an incidence of 30% in Liberia [11]. Ibekwe reported an incidence of 13.5% in Nigeria [14] and Ficenec *et al.* reported an incidence of 17% in Sierra Leone [15]. All these countries are in Lassa fever endemic region in West Africa. Lassa fever related hearing loss has also been reported outside Africa among subjects with imported Lassa fever [17] [18].

Lassa virus induced immunological injury to the structures of the inner ear [9] [19] has been suggested as the initiating cause of hearing loss in Lassa fever in man. An animal study (murine model) has shown that the pathology in the inner ear in permanent hearing loss resulting from Lassa virus infection consists of damage to the cochlear hair cells as well as degeneration of the spiral ganglion cells of the auditory nerve [20]. This could explain the sensorineural hearing loss found in Lassa fever.

Hearing loss impedes interpersonal communication of the affected individual. This in addition to stigma associated with Lassa fever and hearing loss [21] negatively affects the quality of life of the affected person. Thus, every effort aimed at minimizing the incidence of hearing loss in Lassa fever patients is necessary.

In order to successfully combat the health challenges posed by Lassa fever induced hearing loss, it is important to know the exact burden of the hearing loss. It is also important to know how successful treatment of Lassa fever related hearing loss has been in the past.

The aim of this paper is to review the various studies on Lassa fever related hearing loss, in order to assess its incidence and natural course of Lassa fever related hearing loss.

2. Material and Methods

2.1. Search Strategy, Information Sources and Study Selection

Systematic literature review was done on published articles on Lassa fever pa-

tients and Lassa fever survivors. The criteria for inclusion into the review were (a) freely available full text articles published in English from 1969 to 2021; (b) studies on hearing loss among Lassa fever patients which has a minimum sample size of five participants; (c) the method by which the hearing loss was determined must be clearly stated. Articles which fall outside these criteria were excluded from the review.

Internet searches were done using the PubMed and Google Scholar electronic databases. The search terms used were “hearing loss in Lassa fever”, and “treatment of Lassa fever induced hearing loss”. From 35 articles that were initially selected, case reports, duplicate publications and publications on animal studies were screened out. Finally, eight studies which met the inclusion criteria were selected and included in the review.

2.2. Data Extraction and Data Analysis

The data of interest were name(s) of author, country and year of publication, sample size, study design, method of hearing loss determination, age of study participants, and incidence or prevalence of hearing loss. Extracted data from the full text articles were captured on Microsoft Word 2013 and Microsoft Excel 2013. Descriptive statistical analysis was performed on variables relating to self-reported hearing loss and audiometrically determined hearing loss. The analysis was done with Microsoft Excel 2013 and statistical product and service solutions (SPSS) version 22.0, (IBM Corporation, U.S.A). Incidence of hearing loss was expressed as frequency or/and percent (%), gender was expressed as frequency or/and percent (%) and age was expressed in range. The data on the number of Lassa fever patients and Lassa fever survivors and data on hearing loss were pooled to determine the overall mean self-reported hearing loss and the overall mean audiometrically determined sensorineural hearing loss.

3. Results

3.1. Study Characteristics

Eight articles were included in the review. Out of these, one study was done in Liberia [11], three studies were done Sierra Leone [13] [15] [16] and three studies were done in Nigeria [5] [10] [14]. One study published in the United States of America was on missionaries who lived in Africa [12]. In the studies reviewed, the researchers employed two methods of hearing loss determination, self-reported hearing loss and audiometrically determined sensorineural hearing loss. Of the five studies on self-reported hearing loss, one was case-control study while four were cross-sectional studies. The two studies on audiometrically determined sensorineural hearing loss were case-control studies. The details of the various studies are provided in **Table 1**.

The two studies which reported on audiometrically determined sensorineural hearing loss [13] [14] were used in calculating the mean incidence of audiometrically determined sensorineural hearing loss. The five studies which published

Table 1. Studies on Lassa fever associated hearing loss included in the review.

Study	Study location	Number of Lassa cases (n)	Self-reported hearing loss. Participants vs controls (%)	SNHL by audiometry. Participants vs controls (%)
White, 1972 [10]	Nigeria (Northern Nigeria)	23	17.4%	
Mertens <i>et al.</i> , 1973 [11]	Liberia	10	30%	
Frame <i>et al.</i> , 1975 [12]	Missionaries who have lived in Africa	8 missionaries	12.5%	
Cummins <i>et al.</i> , 1990 [13]	Sierra Leone	49		*29% vs 0%
Ehichioya <i>et al.</i> , 2012 [5]	Nigeria (Southern Nigeria).	25	Not reported	
Ibekwe, 2011 [14]	Nigeria (Southern Nigeria).	37		*13.5% vs 0%
Ficenec <i>et al.</i> , 2020 [15]	Sierra Leone	147 Overall Lassa fever 47	*17% vs. 1%	
Li <i>et al.</i> , 2020 [16]	Sierra Leone	31	16%	

Key: SNHL, sensorineural hearing loss. *case-control studies.

self-reported hearing loss [10] [11] [12] [15] [16] were used in calculating the mean incidence of self-reported hearing loss.

3.2. Hearing Loss among Lassa Fever Patients

Lassa fever was first discovered in Nigeria in 1969 [1], but it was not until 1972 that the first report of Lassa fever related hearing loss was published by White [10]. White's report was based on his study of 23 Lassa fever patients who were treated in two hospitals in northern Nigeria [10]. They consisted of 10 males and 13 females aged between 6 and 46 years. Four out of the 23 had hearing loss, and all the four were females. The incidence of hearing loss in that series was 17.4%. For this disease that was hitherto unknown in Nigeria, the study by White was a hospital-based study which provided a detailed clinical and laboratory findings

of which hearing loss was one of them.

The following year, 1973, Mertens *et al.* [11] reported the occurrence of hearing loss in three out of 10 Lassa fever patients aged between 20 and 56 years who were treated in Curran Lutheran Hospital in Liberia. The incidence of hearing loss in their series was 30%.

In 1975, Frame *et al.* [12] published a report on eight missionaries who lived in Africa and had suffered from Lassa fever. They were made up of five males and three females. One patient (12.5%), a male, had hearing loss.

Cummins *et al.* [13] conducted case-control studies on Lassa fever patients in Sierra Leone which were published in 1990. In their first study, audiometry was used to compare the hearing of 49 Lassa fever patients with those of febrile controls. Fourteen (14) Lassa fever patients were found to have sensorineural hearing loss (SNHL), an incidence of 29% compared to 0% in the controls.

In their second study, Cummins *et al.* [13] compared the prevalence of SNHL in Lassa fever seropositive health care workers versus seronegative health care workers, and thirdly, they identified and studied persons with sudden onset of hearing loss.

A study by Ehichioya *et al.* reported in 2012 [5] was conducted in a hospital in Southern Nigeria and it covered the period from November 2005 to February 2008. There were 60 hospitalized suspected cases of Lassa fever, out of which only 29 of them were confirmed to have Lassa fever. Hearing loss was not reported among them.

Ibekwe *et al.* [14] conducted another study in the same hospital that covered the period from July 2007 to April 2009. There were 37 Lassa fever patients aged between 11 and 61 years. Ibekwe *et al.* employed clinical and audiometric assessment in evaluating the hearing functions of their study subjects. Five (5) or 13.5% of the 37 Lassa fever patients had sensorineural hearing loss compared to zero (0%) in the controls.

In their case-control study in eastern Sierra Leone from May 2007 to June 2009, which involved 47 Lassa fever survivors, 29 persons with ordinary febrile illness and 71 controls, Ficenec *et al.* [15] reported a higher incidence of self-reported hearing loss among Lassa fever survivors than among controls (17% vs. 1%). All the cases of hearing loss were females. Using audiometry, there were more cases of bilateral hearing loss among Lassa fever survivors than among the controls (30% vs. 4%).

In another study in Sierra Leone in 2018, Li *et al.* [16] reported a retrospective cross-sectional study on the demographic and clinical presentation of 31 Lassa fever survivors who came for ophthalmic examination. They consisted of eight males and 23 females aged between nine and 70 years. Five (5) out of the 31 had hearing loss, giving an incidence of 16% of self-reported hearing loss. All were females.

In the case-control studies, both self-reported and audiometrically determined, higher incidence of hearing loss was recorded among Lassa fever patients

than among controls [10]-[16] (Table 1). Hearing loss in Lassa fever varied in severity, ranging from mild to profound. There were both unilateral and bilateral cases of hearing loss. Ficenec *et al.* [15] reported 30% cases of bilateral hearing loss, while Cummins *et al.* [13] reported 50% cases of bilateral hearing loss.

Hearing loss persisted in nine (64%) out of the 14 affected patients that were followed up [13].

3.3. Mean Incidence of Hearing Loss

The incidence of self-reported hearing loss in confirmed Lassa fever patients ranged from 12.5% to 30%. The calculated mean incidence of self-reported hearing loss was 17.6%. The incidence of audiometrically determined sensorineural hearing loss in confirmed Lassa fever patients ranged from 13.5% to 29%. The calculated mean incidence of audiometrically determined sensorineural hearing loss was 22.1%.

4. Discussion

4.1. The Incidence of Lassa Fever Related Hearing Loss

The incidence of self-reported hearing loss ranged from 12.5% to 30% with a mean of 17.6%. The incidence of audiometrically determined sensorineural hearing loss ranged from 13.5% to 29% with a mean of 22.1%. Self-reported hearing loss is usually more subjective and cannot characterize hearing loss into sensorineural hearing loss, conductive hearing loss and mixed hearing loss. On the other hand, air- and bone-conduction pure tone audiometry can be used to characterize hearing loss in Lassa fever. Whenever possible, pure tone audiometry should be used instead of self-reporting for better assessment of hearing loss in Lassa fever subjects. The challenge here is the risk of transmission of infection to the technician if the audiometry is done early in the course of the illness. Although most of the cohort studies on Lassa fever related hearing loss were in Lassa fever endemic region of West Africa, Lassa fever related hearing loss has also been reported among patients suffering from imported Lassa fever [17] [18].

The high incidence of hearing loss as well as the high residual rate of hearing loss in those that were followed up makes hearing loss a major challenge in Lassa fever patients. The true burden of Lassa fever related hearing loss would be very difficult to determine for the following reasons. Audiometric screening for hearing loss in Lassa fever patients is not routinely done in most hospitals and relying only on self-report is likely to miss out cases of hearing loss. Also, hearing loss can occur even in subjects with subclinical or trivial Lassa virus infection. Most cases of Lassa virus infection are undiagnosed [3]. This raises the suspicion that some of the so called idiopathic hearing loss in Lassa fever endemic region might actually have been caused by Lassa virus infection.

Study by Meulen *et al.* [22] showed that prevalence of hearing loss was higher among rodent consumers than among non-rodent consumers which indirectly implicated rat in the Lassa virus transmission to man. Any strategy aimed at

combating the challenges of Lassa fever associated hearing loss should also include a strategy for combating Lassa virus transmission from rat to man.

There is presently no effective specific treatment for Lassa fever related hearing loss and no progress has been made in this area going by the available literature. Given the negative physical and psychological impact of hearing loss on the affected individual, future studies should try to address this gap in the management of Lassa fever patients. Also of importance is primary preventive measures aimed at curtailing Lassa virus infection in order to minimize Lassa fever related hearing loss, while hearing rehabilitation should be considered in those with significant hearing loss.

4.2. The Natural Course of Hearing Loss in Lassa Fever

In Lassa fever, improvement in hearing function or resolution of hearing loss can occur spontaneously [13]. However, in some of the Lassa fever patients, the hearing loss still persists after the acute symptoms of Lassa fever have resolved [13]. In the Lassa fever patients with hearing loss that were followed up, the residual rate of hearing loss was high (64%) [13]. Individual case reports of two cases of Lassa fever related sensorineural hearing loss showed that hearing loss was still severe in the two cases one year and four years, respectively, after the initial diagnosis [9]. More prospective cohort studies are required in this area to better understand the natural course of hearing loss in Lassa fever.

The Limitations of the Study

One of the limitations of this study is the small number of studies that evaluated hearing loss audiometrically. The second limitation is that there was only one prospective cohort study in which patients with hearing loss were followed up.

5. Conclusion

Hearing loss remains a major challenge in Lassa fever. The fact that hearing loss can result from imported Lassa fever makes it a disease of public health importance and also a disease of global concern. No effective treatment is available for Lassa fever related hearing loss and not much has been done in this area. This is a very serious gap in the management of Lassa fever related hearing loss which should be addressed in future studies.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

References

- [1] Frame, J.D., Baldwin Jr., J.M., Gocke, D.J. and Troup, J.M. (1970) Lassa Fever, a New Virus Disease of Man from West Africa. I. Clinical Description and Pathological Findings. *The American Journal of Tropical Medicine and Hygiene*, **19**, 670-676. <https://doi.org/10.4269/ajtmh.1970.19.670>
- [2] Rojek, J.M. and Kunz, S. (2008) Cell Entry by Human Pathogenic Arenaviruses.

- Cellular Microbiology*, **10**, 828-835.
<https://doi.org/10.1111/j.1462-5822.2007.01113.x>
- [3] CDC (2014) Lassa Fever. <https://www.cdc.gov/vhf/lassa/transmission/index.html>
- [4] Ihekweazu, C., Saleh, M., Ipadeola, O., Ukponu, W., Sandra, M., *et al.* (2020) Exposure Incidents and Outcome of Lassa Fever Virus (LASV) Infection among Healthcare Workers in Nigeria, 2019. *Journal of Infectious Diseases and Epidemiology*, **6**, Article No. 168. <https://doi.org/10.23937/2474-3658/1510168>
- [5] Ehichioya, D.U., Asogun, D.A., Ehimuan, J., Okokhere, P.O., Pahlmann, M., Olschläger, S., Becker-Ziaja, B., Günther, S. and Omilabu, S.A. (2012) Hospital-Based Surveillance for Lassa Fever in Edo State, Nigeria, 2005-2008. *Tropical Medicine & International Health*, **17**, 1001-1004. <https://doi.org/10.1111/j.1365-3156.2012.03010.x>
- [6] Shaffer, J.G., Grant, D.S., Schieffelin, J.S., Boisen, M.L., Goba, A., Hartnett, J.N., Levy, D.C., *et al.* (2014) Lassa Fever in Post-Conflict Sierra Leone. Viral Hemorrhagic Fever Consortium. *PLOS Neglected Tropical Diseases*, **8**, e2748.
- [7] 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. *The Lancet Infectious Diseases*, **18**, 684-695. [https://doi.org/10.1016/S1473-3099\(18\)30121-X](https://doi.org/10.1016/S1473-3099(18)30121-X)
- [8] Okokhere, P.O., Erameh, C.O., Alikah, F., Akhideno, P.E., Iruolagbe, C.O., Osazuwa, O.O., *et al.* (2018) Acute Lassa Virus Encephalitis with Lassa Virus in the Cerebrospinal Fluid but Absent in the Blood: A Case Report with a Positive Outcome. *Case Reports in Neurology*, **10**, 150-158. <https://doi.org/10.1159/000490374>
- [9] Okokhere, P.O., Ibekwe, T.S. and Akpede, G.O. (2009) Sensorineural Hearing Loss in Lassa Fever: Two Case Reports. *Journal of Medical Case Reports*, **3**, Article No. 36. <https://doi.org/10.1186/1752-1947-3-36>
- [10] White, H.A. (1972) Lassa Fever a Study of 23 Hospital Cases. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, **66**, 390-398. [https://doi.org/10.1016/0035-9203\(72\)90269-6](https://doi.org/10.1016/0035-9203(72)90269-6)
- [11] Mertens, P.E., Patton, R., Baum, J.J. and Monath, T.P. (1973) Clinical Presentation of Lassa Fever Cases during the Hospital Epidemic at Zorzor, Liberia, March-April 1972. *The American Journal of Tropical Medicine and Hygiene*, **22**, 780-784. <https://doi.org/10.4269/ajtmh.1973.22.780>
- [12] Frame, J.D. (1975) Surveillance of Lassa Fever in Missionaries Stationed in West Africa. *Bulletin of the World Health Organization*, **52**, 593-598.
- [13] Cummins, D., McCormick, J.B., Bennett, D., Samba, J.A., Farrar, B., Machin, S.J. and Fisher-Hoch, S.P. (1990) Acute Sensorineural Deafness in Lassa Fever. *JAMA*, **264**, 2093-2096. <https://doi.org/10.1001/jama.264.16.2093>
- [14] Ibekwe, T.S., Okokhere, P.O., Asogun, D., Blackie, F.F., Nwegbu, M.M., Wahab, K.W., Omilabu, S.A. and Akpede, G.O. (2011) Early-Onset Sensorineural Hearing Loss in Lassa Fever. *European Archives of Oto-Rhino-Laryngology*, **268**, 197-201. <https://doi.org/10.1007/s00405-010-1370-4>
- [15] Ficenec, S.C., Percak, J., Arguello, S., Bays, A., Goba, A., Gbakie, M., Shaffer, J.G., *et al.* (2020) Lassa Fever Induced Hearing Loss: The Neglected Disability of Hemorrhagic Fever. *International Journal of Infectious Diseases*, **100**, 82-87. <https://doi.org/10.1016/j.ijid.2020.08.021>
- [16] Li, A.L., Grant, D., Gbakie, M., Kanneh, L., Mustafa, I., Bond, N., Engel, E., *et al.* (2020) Ophthalmic Manifestations and Vision Impairment in Lassa Fever Survivors. *PLOS ONE*, **15**, e0243766. <https://doi.org/10.1371/journal.pone.0243766>
- [17] Raabe, V.N., Kann, G., Ribner, B.S., Morales, A., Varkey, J.B., Mehta, A.K., *et al.*

- (2017) Favipiravir and Ribavirin Treatment of Epidemiologically Linked Cases of Lassa Fever. *Clinical Infectious Diseases*, **65**, 855-859. <https://doi.org/10.1093/cid/cix406>
- [18] Macher, A.M. and Wolfe, M.S. (2006) Historical Lassa Fever Reports and 30-Year Clinical Update. *Emerging Infectious Diseases*, **12**, 835-837. <https://doi.org/10.3201/eid1205.050052>
- [19] Cashman, K.A., Wilkinson, E.R., Zeng, X., Cardile, A.P., Facemire, P.R., Bell, T.M., Bearss, J.J., Shaia, C.I. and Schmaljohn, C.S. (2008) Immune-Mediated Systemic Vasculitis as the Proposed Cause of Sudden-Onset Sensorineural Hearing Loss following Lassa Virus Exposure in Cynomolgus Macaques. *mBio*, **9**, e01896-18. <https://doi.org/10.1128/mBio.01896-18>
- [20] Yun, N.E., Ronca, S., Tamura, A., Koma, T., Seregin, A.V., Dineley, K.T., Miller, M., *et al.* (2015) Animal Model of Sensorineural Hearing Loss Associated with Lassa Virus Infection. *Journal of Virology*, **90**, 2920-2927. <https://doi.org/10.1128/JVI.02948-15>
- [21] Chime, P.E., Okoli, P.C., Chime, E.N., Anekpo, C.C., Ozougwu, A.O. and Ofojebe, P.C. (2022) Diseases Associated With Stigma: A Review. *Open Journal of Psychiatry*, **12**, 129-140. <https://doi.org/10.4236/ojpsych.2022.122011>
- [22] Meulen, J.T., Lukashevich, I., Sidibe, K., *et al.* (1996) Hunting of Peridomestic Rodents and Consumption of Their Meat as Possible Risk Factors for Rodent-to-Human Transmission of Lassa Virus in the Republic of Guinea. *The American Journal of Tropical Medicine and Hygiene*, **6**, 661-666. <https://doi.org/10.4269/ajtmh.1996.55.661>