A REVIEW OF LASSA FEVER OUTBREAKS IN NIGERIA FROM 1969 TO 2017: EPIDEMIOLOGIC PROFILE, DETERMINANTS AND PUBLIC HEALTH RESPONSE

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ABSTRACT

Introduction: Lassa fever outbreaks have occurred in Nigeria since the 1969 till date. This is in spite of the fact that the reservoir and modes of transmission have been known for all these years. This review aimed at describing the epidemiology and determinants of the Lassa fever outbreaks in Nigeria from 1969 to 2017 and the public health response to these outbreaks.

Method: The guidelines for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were used to conduct the review between May 2017 and January, 2018. We searched PubMed, Science direct, WHO library databases and Google Scholar for articles published from 1970 till January 2018. Other relevant websites such as those of the World Health Organization, Nigeria Centers for Disease Control and Prevention were searched for Lassa fever outbreak reports.

Results: Twenty-six articles and reports were included in the final review. These described twenty-one outbreaks involving 5442 suspect cases, 768 confirmed cases and 631 deaths from suspected or confirmed Lassa fever. Thirty-two states and the Federal Capital Territory have ever recorded outbreaks of Lassa fever. Lassa fever cases now occur in various states in Nigeria all year round with dry season peaks. Nosocomial transmission has remained a consistent determinant. Public health responses have changed over time starting from predominantly case management in initial outbreaks to a centrally coordinated response supporting states and institutions over the years.

Conclusion; Lassa fever outbreaks have increased in frequency and geographic spread with case fatality ratio remaining unacceptably high. The same determinants have persisted with nosocomial transmission a consistent factor. Public health response has consistently improved with the last two years showing the most coordinated response.
We recommend that the definition of Lassa fever in the Nigerian Integrated Disease Surveillance and Notification System (IDSR) be revised to reflect the current reality to ensure better Lassa fever control.

Key words: Lassa fever, Outbreak, Viral haemorrhagic fevers, Nigeria.

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INTRODUCTION

Lassa fever is an acute viral haemorrhagic fever caused by the Lassa virus, a single stranded RNA virus of the are naviridae family[1,2,3] It is a zoonotic disease transmitted to man through contact with the natural host, the multi-mammate rat called Mastomysnatelens is in which it persists as a lifelong and mostly silent infection.[4,5]Lassa fever is also transmitted from man to man through contact with body fluids of infected persons.[5]

The disease was first identified in 1969 in Borno state, Nigeria, following the death of two medical missionaries and infection of a third one.[6,4] The cause of their illnesses was eventually found to be Lassa virus a disease named after the town Lassa in Nigeria where the first cases were isolated.[6] Since then, it has been shown that Lassa fever is endemic in Nigeria with the prevalence of antibodies to the virus being approximately 21% in the Nigerian population.[7] Lassa virus infects 100,000 to 300,000 people annually in West Africa, kills 5,000 to 10,000, and leaves approximately 30,000 people deaf. In West Africa, mainly Nigeria, Sierra Leone, Guinea and Liberia it causes 10% to 15% of adult febrile admissions to the hospital and a suspected 40% of non-surgical deaths.[4,8]

The signs and symptoms of Lassa fever occur 1-3 weeks after the patient comes into contact with the virus[9] About 80% of Lassa fever infections present with mild symptoms and

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are often undiagnosed. Mild symptoms include slight fever, general malaise and weakness, and headache. In 20% of infected individuals, the disease may progress to more serious symptoms.[9] The case fatality rates observed among patients hospitalized with severe cases of Lassa fever is between 15 - 20%and this can get to up to 50% in some outbreaks.[10,11]

A special report in the Lancet signposts increased funding for the National Institute for Allergy and Infectious Disease and its blueprint for research, including Lassa fever. This high profile pointer shows that understanding of Lassa fever control and treatment has assumed a higher profile making this a critical time for a concerted international effort to achieve these ends.[12]

This review aimed at describing the epidemiology and drivers of the Lassa fever outbreaks in Nigeria from 1969 to 2017 and the public health response to these outbreaks. Lessons learnt from these outbreaks need to be applied in preventing future outbreaks and responding to outbreaks if they occur.

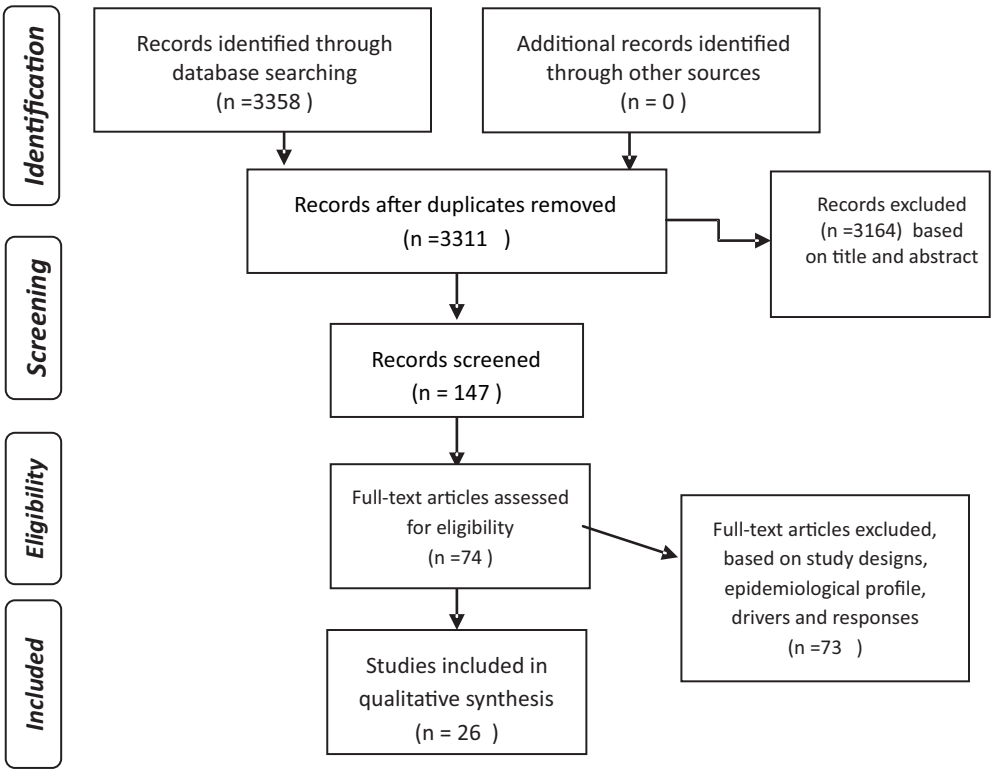
METHOD

Search strategy (search terms, processes and results)

The guidelines for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) was used to conduct a systematic search for original research reports of Lassa fever outbreaks in Nigeria. The search and review strategy are detailed in Figure 1.

Prisma Process.[13] The search was conducted between May 2017 and January, 2018. We searched PubMed database, Science direct, WHO library databases and Google Scholar for articles published from 1970 till January, 2018. The main themes considered were Lassa fever outbreaks in Nigeria, the epidemiological profile, the determinants and the public health responses. Other relevant websites such as those of the World Health Organization, Nigeria Centers for Disease Control and Prevention were searched for outbreak reports. The WHO and NCDC reports that contained all information on each reporting year were the ones that were included in the review.

Figure 1: The PRISMA process for literature search



Data Abstraction and Synthesis

The data abstraction and synthesis process were conducted by two research team members (KW and CN) independently. Discordant decisions were resolved by consensus and when no consensus was reached, a third person (TJ) made a contribution and the majority view was adopted.

Data abstraction and synthesis included the following 4 steps: identification, screening, eligibility, and inclusion. During the identification step, articles were identified using the search strategy described above. Titles and abstracts were then screened to determine their relevance to our study objectives. During the eligibility step, the full texts of the articles were reviewed.

Details of information relevant to our research questions were extracted and tabulated according to; outbreak year, time of year (month), states and Local Government areas affected, persons affected, laboratory confirmation, mortality, case fatality rates and public health response. Studies were then categorised by epidemiology, determinants and public health response.

Inclusion and Exclusion Criteria

The key inclusion criteria were articles that focused on; Lassa fever outbreak description, description of the epidemiology of the outbreak and Lassa fever outbreak response. Exclusion criteria were articles that described outbreaks outside Nigeria and those that described studies conducted in animals. Observational and qualitative studies were considered for inclusion when they clearly described a Lassa fever outbreak.

RESULT

The initial search generated 3358 results. After removal of duplicates, 3311 articles and reports remaining were screened based on titles and abstracts resulting in the further exclusion of 3164 papers. Content review of the 147 full texts articles and reports led to the exclusion of an additional 73 papers. Further screening of the remaining 74 full text articles and reports led to the exclusion of another 48 articles. The main reasons for exclusion were based on study designs, epidemiological profiles, determinants and public health responses. Finally, a total of twenty six (26) articles and reports were included in the final review. These twenty six articles and reports described a total of twenty (21) outbreaks in the period 1969 to 2017.

Table 1: Summary of reviewed articles and reports on Lassa fever outbreaks in Nigeria from 1969 to 2017

Outbreak year	Reference	Study design
1969	(6) (4) (14)	Review article Book Review article
1970	(15) (16) (4)	Case series reports Case series reports Book
1974	(17)	Case Series Reports
1975	(18)	Review Article
1989	(19)	Case series reports
1993	(20)	Case series report
1994	(18)	Review Article
1995	(18)	Review Article
1998	(18)	Review Article
1999	(18)	Review Article
2000	(18)	Review Article
2002	(1) (2) (21) (18)	Retrospective study Review Article Retrospective Study Review Article
2003	(1) (2) (21) (18)	Retrospective study Review Article Retrospective Study Review Article
2004	(1) (2) (21) (18)	Retrospective study Review Article Retrospective Study Review Article
2005	(22) (18)	Retrospective Study
2006	(22) (18)	Retrospective
2009 – 2010	(2) (23) (24)	Review article Review article Outbreak report
2012	(2) (25)	Review Article Outbreak report
2015	(26)	Outbreak report
2015 – 2016	(27) (28)	Outbreak report Case series report
2016 – 2017	(27)	Outbreak report

Epidemiology of the Lassa fever outbreaks
The epidemiology of the Lassa fever outbreaks is summarised in Table 2.

Person
Our review showed that between 1969 and 2017, five thousand, four hundred and forty-two (5442) suspect cases, 768 confirmed cases and 631 deaths from presumptive or confirmed Lassa fever were recorded. The highest number, one thousand and twenty-two (1022) cases, were reported in the 2016-2017outbreak. A total of 40 health care worker deaths were reported in the 21 outbreaks. The materials we reviewed did not demonstrate any predilection for any particular age group or sex. The highest case fatality rate was 58.1% reported in the 2003 outbreak.[1,2,21]

Table 2: Reported Lassa fever outbreaks showing states affected, cases and deaths in Nigeria 1969-2017

Outbreak year	States	Cases	Deaths	Case fatali ty rates (%)	Healthcar e workers deaths	Laboratory Confirmed	References
1969	2	4	2	50	3	2	(6) (14)
1970	1	28	13	46.43	1	13	(15)
1974	1	3	1	33.3	2	3	(17)
1975	1	1	1	100	-	-	(18)
1989	2	34	22	65	9	11	(19)
1993	1	400	15	3.8	5		(20)
1994	4	77	13	16.9			(18)
1995	5	69	--	--			(18)
1998	2	3	--	---			(18)
1999	1	46	--	--			(18)
2000	2	86	26	30.23			(18)
2002	1	56	15	26.8			(1)(2)(21)(18)(25)
2003	1	31	18	58.1			(1)(2)(21)(18)
2004	1	50	21	50			(1)(2)(21)(18)
2005	3	36	16	44.4			(22)(18)
2006	1	19	1	5.3			(22)(18)
2009 – 2010	15	200	50	25	4	25	(2)(23)
2012	23	937	95	10.14	6	148	(2)(25)
2014	13	989	36	3.64%		110	(26)
2015	14 states and FCT	430	40	9.3		25	(27)
2016	23 (28)	921	119	12.9	10	109 (101)	(27) (28)
2017	19 (29)	1022	127	12.8 (28.6 in confirmed and probable and 124% for all cases)		322 (143) (14) probable)	(29)
Total		5,442	631		40	768	

Place

Between1969 and December 2017, thirty-two (32) states and the Federal Capital Territory (Abuja) recorded outbreaks of Lassa fever. The state that has recorded the most outbreaks is Edo state followed by Plateau and Nasarawa states. Early outbreaks (1969 – 1993) were mainly around the northern Nigeria with just occasional eastern Nigerian states recording cases, however, from around 1994 Edo state started recording outbreaks and is currently the state with the highest number of outbreaks. Currently, all regions of Nigeria now have states reporting cases.

Figure 2: States with outbreaks recorded 1969-1979 in Nigeria

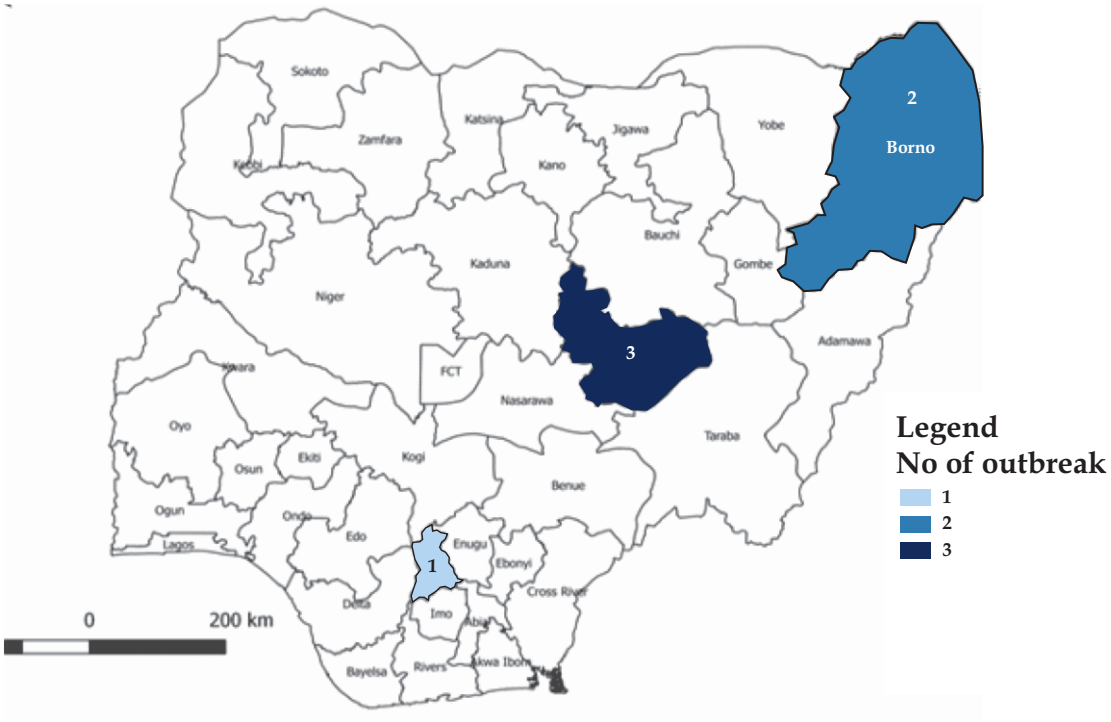


Figure 3: States with outbreaks recorded 1980-1989 in Nigeria

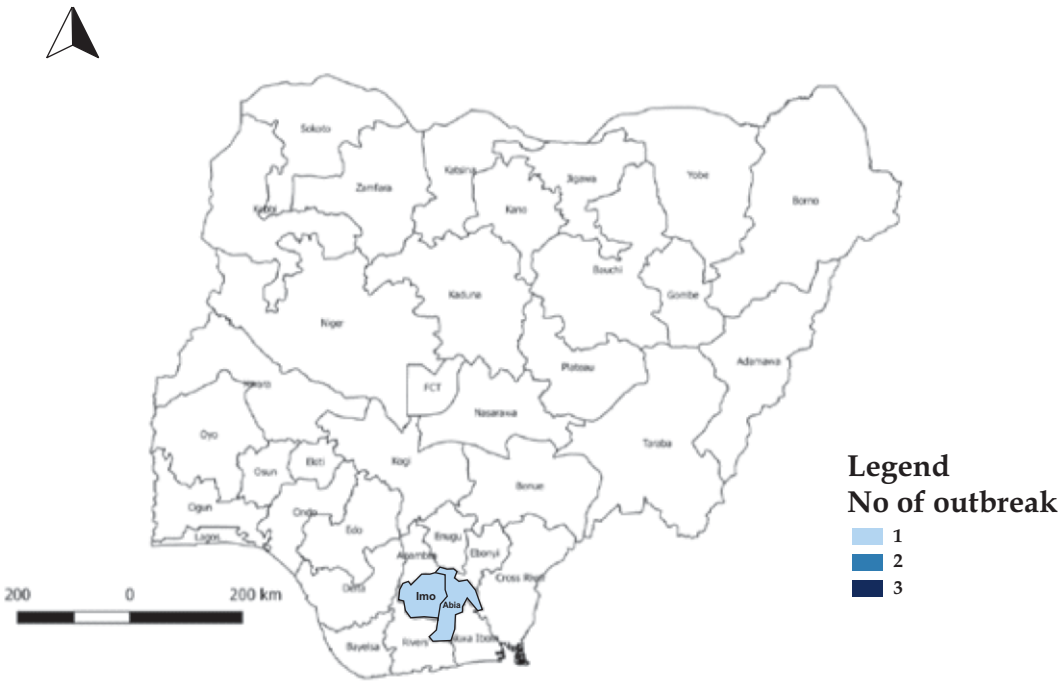


Figure 4: States with outbreaks recorded 1990 - 1999 in Nigeria

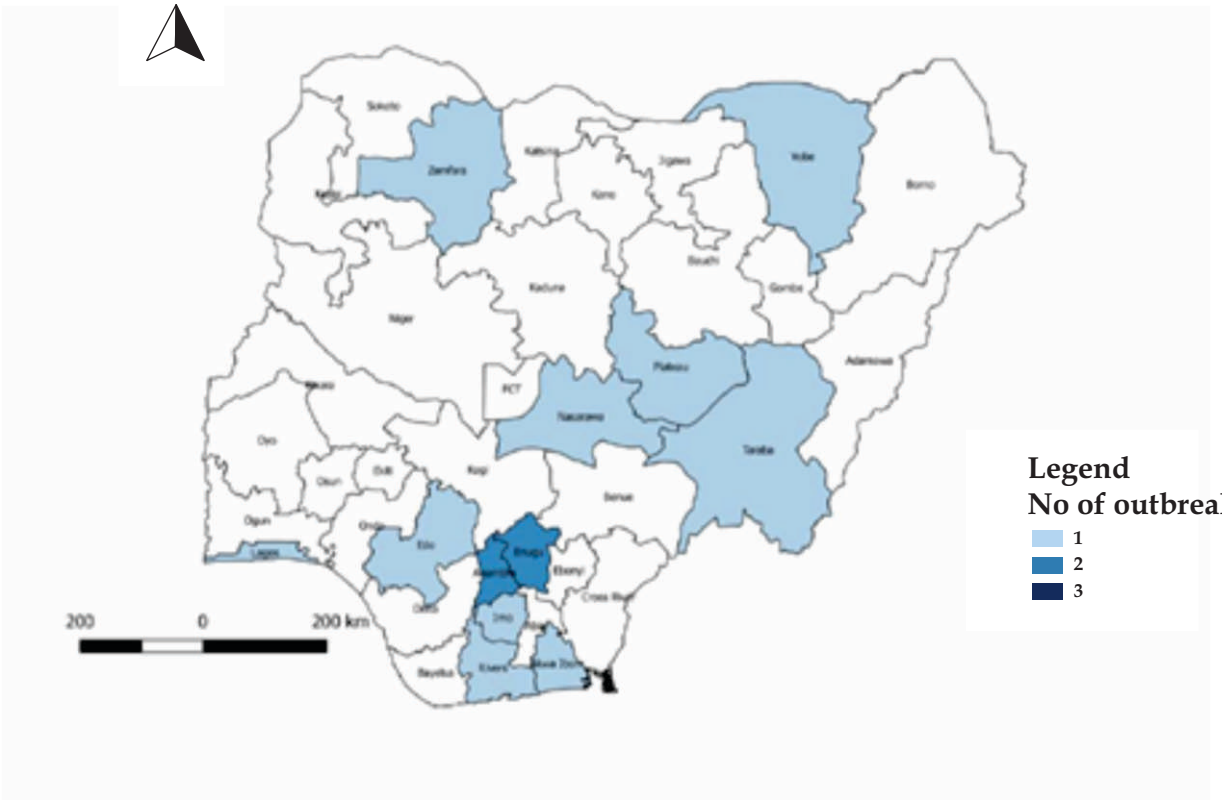


Figure 5: States with outbreaks recorded 2000 - 2009 in Nigeria

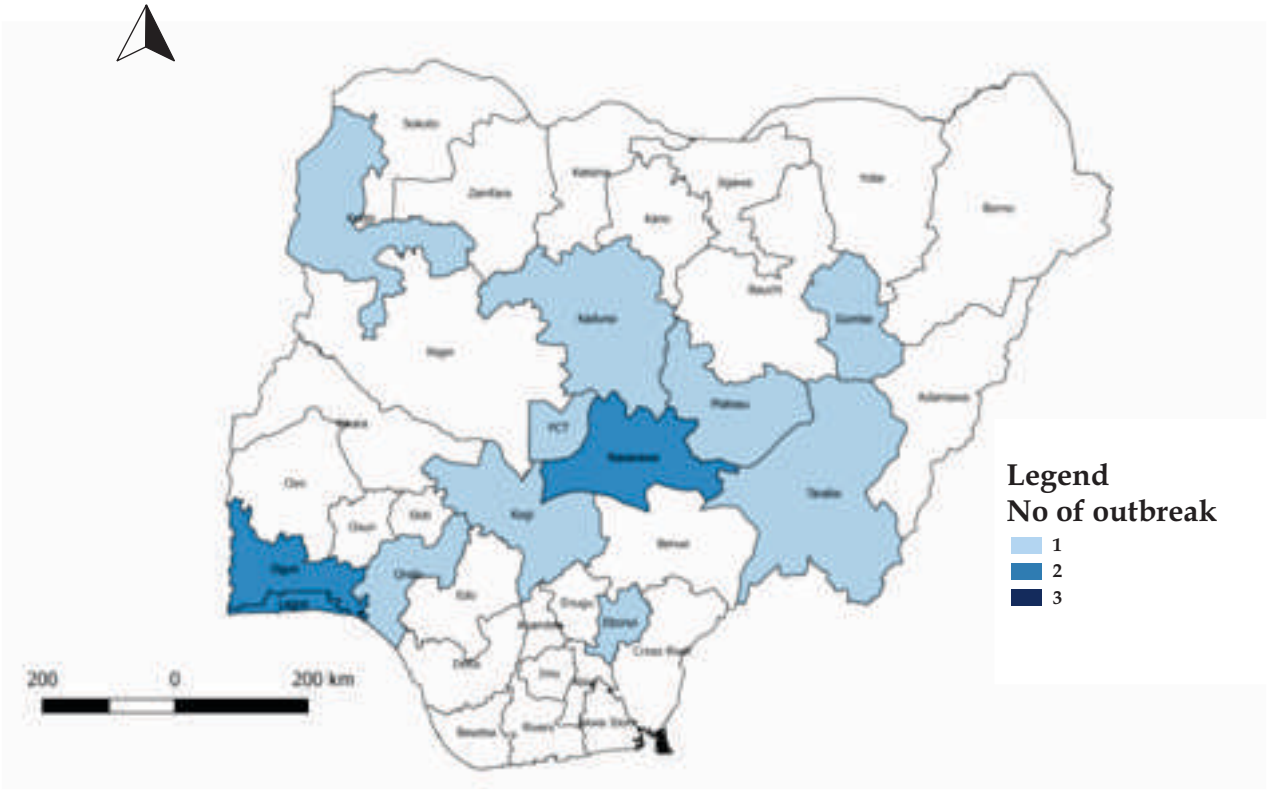
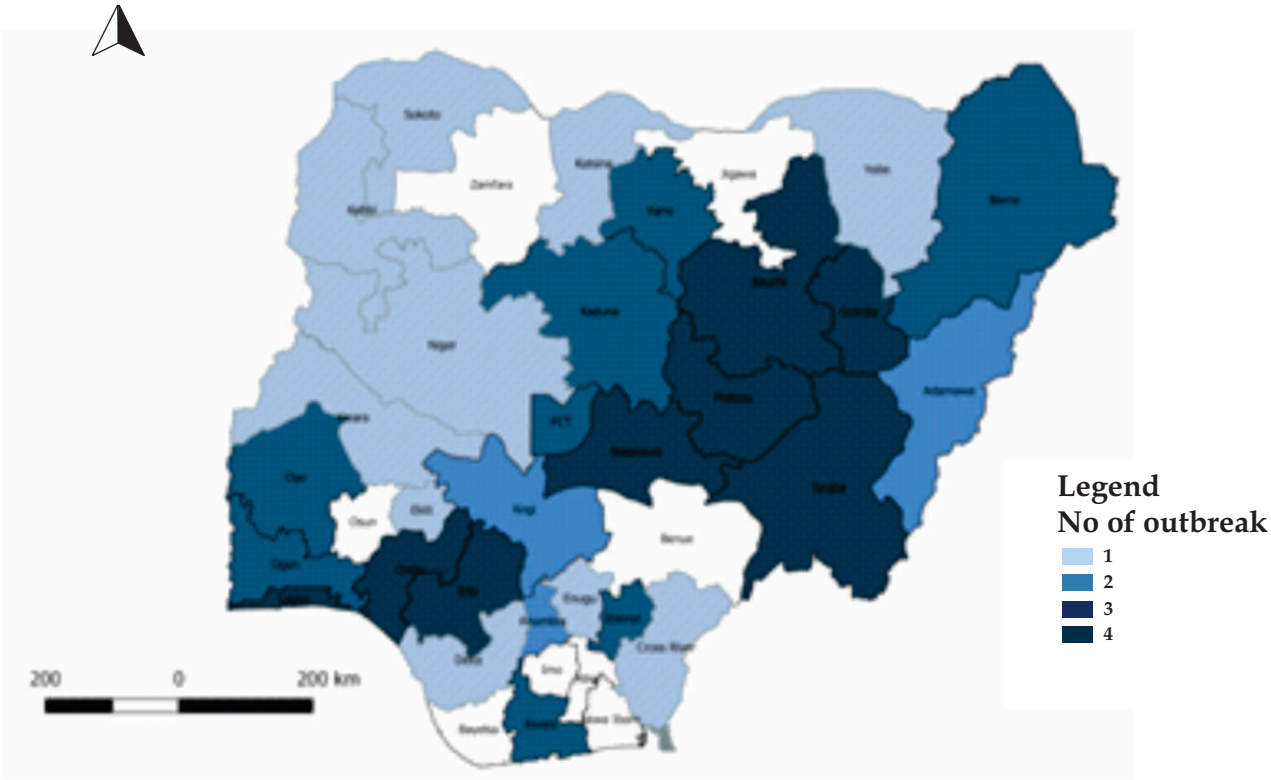


Figure 6: States with outbreaks recorded 2010 - 2017 in Nigeria



Time

From 1969 to 2017 outbreaks have been reported in every decade. However, in 1980-1990, only one outbreak was reported towards the end of the decade (1989) subsequently between 1990 and 2010, an average of 5.5 outbreaks was recorded per decade and thereafter outbreaks were reported almost every year from 2010 to 2017. Between 1969 and 1989 the reported outbreaks occurred between December and March (corresponding to roughly within the end of the rainy season and the beginning of the dry season), however, from around 2003, the outbreaks started around November and December and extending up to May/June. Recently as shown in the 2015-2017 outbreaks, cases have been identified all through the year with the 2015-2016 outbreak stretching from August 2015 through December, 2016 to December, 2017.

Figure 7: Trends of Lassa fever outbreaks in Nigeria 1969 to 2017.

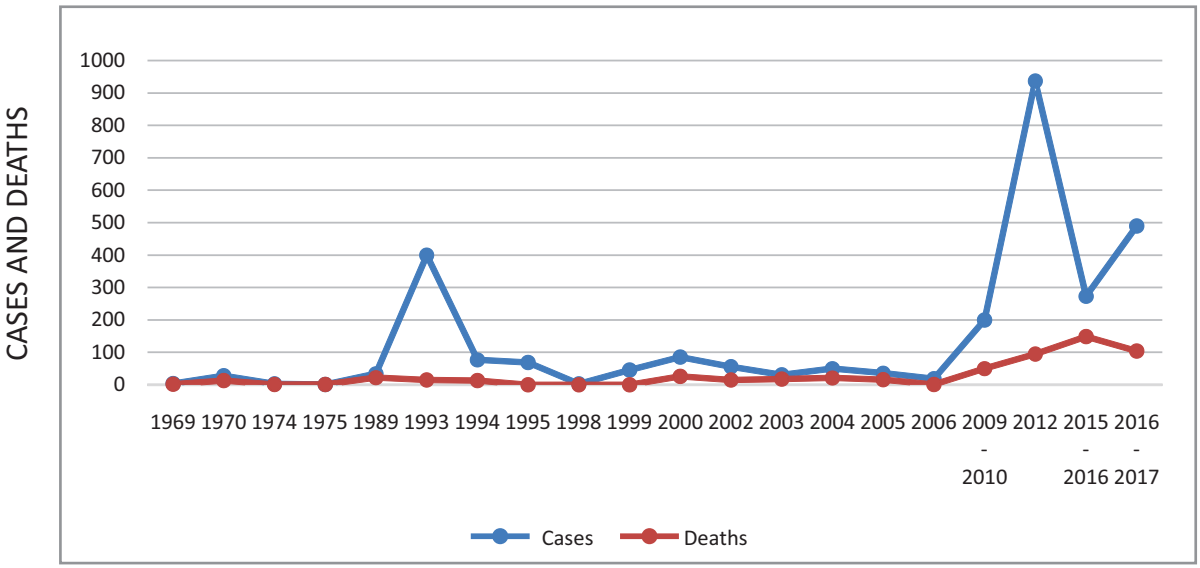


Figure 8: Seasonality of reported Lassa fever outbreaks in Nigeria, 1969 to 2017.

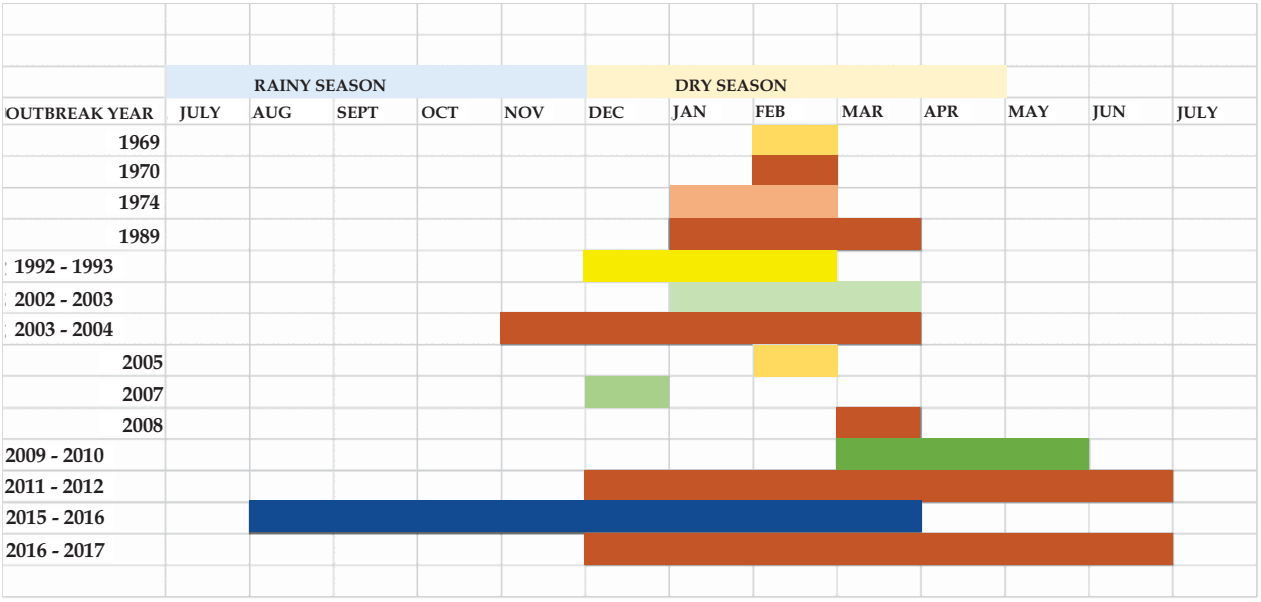


Table 3: Reported driving factors of Lassa fever outbreaks in Nigeria 1969 to 2017

Outbreak year	Inference	Reference
1969	• First case in the country • Low index of suspicion hence • No knowledge of the epidemiology	(4)
1970	• No awareness and epidemiologic knowledge of disease • Nosocomial transmission	(15) (14)
1974	• Nosocomialtransmission • Lack of strict isolation procedures	(17)
1989	• Outbreak hospitals were inadequately equipped and staffed • Poor medical practice • Parenteral drug rounds with sharing of syringes, conducted by minimally educated and supervised staff • Nosocomial transmission	(19)
1993	• Hunting of rat was a cause of rodent to person transmission • Rats were found trapped in victims' homes • Bush burning for hunting and improper food storage • Poor knowledge of health workers on epidemiology of Lassa fever • Poor medical practice • Unavailability of drugs for treating Lassa fever • No isolation wards	(20)
2002 to 2004.	• Prolonged dry season • Ribavirin is not always available in the hospital • Poor laboratory capacity for specialised test for Lassa fever • Poor funding of hospitals	(1)
2005 to 2008	• Prolonged dry seasons with ongoing rodent to human transmission and • Nosocomial transmission • Overcrowded semi urban settlements • No available local laboratories for case and contact management • Early diagnosis and prompt treatment difficult • Poor hospital capabilities for infection control	(2)(23)
2009 to 2010	• Poor hospital infection control mechanisms and emergency preparedness • High health workers susceptibility and outbreak transmission. • Poor hospital capabilities and funding	(23)
2012	• Presentation of index case as an emergency surgical case • Poor infection control system • Poor hospital capabilities to prevent outbreaks	(25)
2015 to 2016	• Population density and displacements of people (Internally displaced persons) • Political instability and insecurity • Cultural beliefs affecting both reporting and response time to outbreaks • Health system capacity: Most health facilities in rural areas lack proper equipment for diagnosing the disease. • Lack of capacity in most states to contain the outbreak • Poor infection control measures like barrier nursing and personal protective equipment	(28)

Table 4: Outbreak investigation and response in Nigeria 1969 to 2017

Outbreak year	Inferences	References
1969	• Virus isolation and identification of the Lassa virus • Case management with supportive therapy with fluids, antimalarial and antibiotics	(4)
1970	• Confirmation of Lassa fever using complement fixation test • Identification of household contacts of patients	(30)
1974	• Contact tracing and serosurveys • Laboratory investigation by Complement fixation to test • Collaboration between local Hospital University of Nigeria Teaching Hospital (UNTH) and Federal Ministry of Health (FMOH) (indicating some level of central coordination)	(17)
1989	• National and regional investigation by the UNTH Enugu and (FMOH) retrospectively • Case finding done between December 1988 to March 1989 through careful analysis of records and in patient's deaths in all deaths in AbohMbaise, Aba and Owerri • Laboratory confirmation was by either or both the isolation of Lassa virus and the detection of IgG and IgM by immunofluorescent antibody assays against standard Lassa virus and isolates from this epidemic. • Interviews were completed on 935 individuals and 814 serum samples were obtained	(19)
1993	• National response team conducted community and hospital serosurveys with aid from Jos University Teaching Hospital. • Analysis of hospital responsiveness and emergency preparedness. • Assessment of community cultural and social practices	(20)
2002 to 2004	• Response was with Irrua Specialist Teaching Hospital [ISTH], collaboration with virology center Lagos and BNI Germany, for hospital based serosurvey of Lassa fever from 2001 to 2004. • Use of Ribavirin in treatment of confirmed cases.	(1) (21)
2005 to 2008	• Case management by the use of Ribavirin, supportive treatment with fluid, antibiotics. • Local, national and international collaboration on retrospective serosurveys among the states of the outbreaks	(2) (23)
2009 to 2010	• Collaboration with State Ministry of Health and FMOH for urgent serosurveys, diagnosis and treatment. • Case management was by the use of Ribavarin	(23)
2012	• Effective coordination • Laboratory testing, • Active surveillance, • Community mobilization, • Contact and suspect case evaluation and • Case management	(25)
2015 to 2016	• EOC activated at national level • Coordination with WHO, NCDC and FMOH, Surveillance (including active surveillance and contract tracing), • Case management, • Infection prevention and control, and • Sensitization of community and health workers	(26)
2017	• EOC activated nationally and in affected states • Coordination: nationally, state level and also at Local Government Area, constit ution of rapid response teams where it didn't exist) • Surveillance • Case management/infection control • Laboratory capacity provided • Logistics coordinated centrally also supporting states • Risk communication/Social mobilization • VHF case-based forms completed by affected States • National VHF guidelines (National Viral Haemorrhagic Fevers Preparedness guidelines, Infection Prevention and Control of VHF and Standard Operating Procedures for Lassa fever management) are available on the NCDC website- http://ncdc.gov.ng/diseases/guidelines	(31)

DISCUSSION

We set out to review the literature to determine the epidemiology, drivers and public health response to Lassa fever outbreaks in Nigeria from 1969 to the end of 2017. The findings of our review show that over the years, Lassa fever outbreaks have increased in frequency and geographic spread with case fatality ratio remaining unacceptably high: 50% in early outbreaks to 51.57% in the 2015-2016 outbreak.

The trend of reported outbreaks appeared to

show that no outbreak was reported between 1980 and 1990 in contrast with the turn of the century year 2000 when outbreaks were reported almost every year. Some factors that may be responsible for the quiet decade may be the fact that this was the period when the public health infrastructure completely collapsed under the military era with very weak central coordination compared to the era from year 2000 when Nigeria got back under civilian rule.

It now appears that Lassa fever cases occur in various states in Nigeria all year round albeit with a peak around the dry season. With this pattern, one wonders if the definition of an outbreak as defined in the integrated disease surveillance and notification/disease surveillance and notification (IDSR/DSN) system[31] can still be applied to this disease in Nigeria. It may be more prudent to consider it an endemic disease with high rate of transmission and case fatality. This may make it something that allows the disease to be mainstreamed and taught to every health worker to suspect and rule out for every febrile patient. Researchers in Irrua Edo state had a more detailed description of the seasonality describing two levels of seasonality a high Lassa fever incidence in the hospital from November through March (dry season) and low incidence from April through October (rainy season).[32] This dry season peak observed in the reports is similar to what has been reported in literature on the seasonality of Lassa fever.[12] This is important in planning and preparedness, going by the reported months, that mid-end of the rainy season (June-August) is a good time to engage communities in social mobilization and also to organize yearly refresher trainings for healthcare workers as well as preposition case management stock.

The highest number of cases was recorded in the 2016-2017 outbreak, when this is superimposed on the outbreak response, it begins to show that an explanation for this may be the increase in central coordination with active case search and more focused contact management which will obviously yield more cases.

From the literature we reviewed, the persons were not well reported so we could not make out any clear age or sex predilection highlighting the need to identify clearly who is infected in these cases. Our review shows that medical personnel involved in direct patient care, surgery, pathology, and laboratory testing of clinical specimens have a high risk of infection[14] with surgeons appearing to be a high-risk group indicating gaps in surgical infection prevention and control. This fact has been apparent since 1974 when it was reported that in Onitsha, a physician may have been infected while performing surgery for relief of tracheal obstruction in a patient with Lassa fever with this procedure resulting in a heavy shower of respiratory droplets.[14,33,17]

Most reports did not show attack rates and case fatality rates among healthcare workers also there was no report that showed when all cases were confirmed or the number of suspect cases that turned out not to be false positives. This information will be helpful in validating the criteria used in classifying a case as suspect (i.e. give an indication of the sensitivity or specificity of the suspect case definition). There was hardly any information on what happened to the contacts in most of the papers and no outcomes for them could be conclusively deduced. No report mentioned much about how the dead bodies were handled. Another major gap observed in the reports especially the NCDC weekly epidemiologic report was that healthcare worker deaths are not reported as a separate entity it is usually lumped together with other deaths there was also no clear description of the age, sex and occupation of the cases. It is important that this is clearly reported as it has implications for interpreting and understanding the

outbreaks as well as understanding the drivers such as nosocomial transmission.

The reports of states affected appears to move from north central Nigeria in the early outbreaks moving through Onitsha, East Central State, Nigeria in 1974 thus extending the known area of occurrence of Lassa virus to southern Nigeria[17] and moving towards Mid-western to cover eastern and western Nigeria. It will be instructive to explore the factors and things that changed over the years to result in this pattern we observed. Also, it will be good to find out what is peculiar with Edo state that made it the state with the highest number of outbreaks despite the fact that the first outbreak reported was in 1994. The state is now considered a hotspot for Lassa fever in Nigeria.[34] Certain cultural and personal habits have been implicated as factors promoting high incidence of Lassa fever in Edo State. These factors included use of rat meat as a source of protein by people in some communities, contamination of exposed food by rat faeces and urine, and traditional autopsy, where the operator may be injured with scalpel and the injury contaminated with the blood of the deceased.[35] Other risk factors identified included forceful ingestion of water used in bathing a dead husband by a widow suspected to be involved in his death and practices of drying Garri (cassava flour) in the open air, where Lassa fever infected rodents contaminate the Garri while using it as a food source.[34]

Some driving factors have remained consistent whereas others had changed over time from ignorance of the disease in the early 1970's to political instability in the 2010's. The first documented outbreak of Lassa fever was hospital associated and took place in 1969 in Jos, northern Nigeria[9] and since then, nosocomial transmission has remained a consistent driving factor in all the outbreaks indicating poor infection prevention and control in health facilities.[36] It is unacceptable that nearly 50 years after this virus was identified and killed healthcare workers, the same pattern still occurs even after researchers have pointed this unacceptable fact out 22 years ago.[33]

A good public health response to a Lassa fever outbreak involves coordination, surveillance, case management/infection control, laboratory support, logistics management and risk communication/social mobilization.[37] Public health responses have also changed over time starting from predominantly case management in initial outbreaks to a centrally coordinated response supporting states and institutions over the years. Two public health responses that have not been clearly documented are social mobilization and rodent control measures. Central coordination started becoming apparent from around the year 2012, prior to that period, reports alluded to some sort of collaboration between the federal, state and hospital management.[25] The clear public health response that reflected all the aspects necessary for a robust public health response emerged in the 2015-2016 outbreak. This was also the first outbreak report in which infection prevention and control was specifically mentioned as part of the response as well as social mobilization. The outbreak of 2017 has the most coordinated public health response with the NCDC weekly epidemiologic report clearly outlining actions undertaken in the following areas coordination, surveillance, case management/infection control, laboratory support, logistics management and risk communication/social mobilization.[31.]

One major factor that was constantly reported as a factor negatively impacting the response was laboratory confirmation of cases. Majority of reports mentioned that cases were confirmed at Irrua Specialist Teaching Hospital (ISTH). There are currently very few centres where laboratory confirmation of Lassa fever can be done in

Nigeria.[2] This figure is highly unacceptable for an endemic disease of such public health importance (prone to outbreaks, high case fatality rate, nosocomial and community transmission and serious sequelae i.e. deafness and stigmatization for those that survive). The nation needs many more centres that can quickly confirm Lassa fever in order to reduce the turnaround time of results from laboratories to clinicians or the community where they are needed. This point still supports our position that Lassa fever has to be moved from the realm of some exotic disease to one that is endemic, highly infectious and pathogenic and with serious sequealae that requires resources to prevent, diagnose, treat and rehabilitate at all states and at all areas. Good laboratory support is also important in genetic typing that can help show clearly if the source of infection is linked or coming from different sources.[25,38]

In Nigeria, awareness of Lassa fever among health workers is still low in some areas and high in some. Lassa fever can present like other common febrile such as malaria, tonsillitis and typhoid fever this could make clinicians to continue with malaria treatments as thus resulting in delayed diagnosis of Lassa fever.[39] There is a need to train and retrain health care workers generally along that line and encourage them to have a high index of suspicion for Lassa fever. Availability of point of care rapid diagnostic tests for Malaria will help in reducing this confusion in diagnosis.

Another major gap observed in the literature search was that there was no single report that summarized any particular outbreak so there was no comprehensive outbreak report detailing what happened in all the states and to all suspect and confirmed cases for the different outbreaks. Most of the reports were on individual case/cases in different centres with the Nigeria Centre for Disease Control epidemiological reports giving weekly updates but no clear indication of when an outbreak was declared over with a comprehensive report of the outbreak response. This may be an indication that cases never really ceased further buttressing our earlier point that there may be a need to relook the definition of Lassa fever outbreak in the Nigerian context in order to come up with an approach/response to Lassa fever that works and that will allow better development of knowledge and infrastructure necessary to control this disease. There was hardly any report that focused on what happened in communities and this is a major gap. This may be an indication of the lack of central coordination seen in most of the reported outbreaks. One factor that was never clearly resolved in all the reported outbreaks was the source of infection for almost all the index cases. No clear answer as to how the first rodent to man transmission occurred. This should be given more attention as it would help in devising best strategies for community control of Lassa fever.

CONCLUSION

The findings of our review show that Lassa fever outbreaks have increased in frequency and geographic spread over the years with case fatality ratio remaining unacceptably high: 50% in early outbreaks to 51.57% in the 2015-2016 outbreak. Recent outbreaks now show that cases occur all year round across almost all the regions of the country. The review did not show any clear description of person commonly affected, but did show an increasing trend, wider geographical spread over the years. The same determinants have persisted over the last 48 years with nosocomial transmission a consistent factor in all the reported outbreaks. Public health response has consistently improved over the years with the last two years showing the most coordinated response. There is a need to relook the definition of Lassa fever outbreak in the Nigerian context to see how well it has served the nation in informing Lassa fever control as a whole in order to come up with an

approach/response to Lassa fever that works and that will allow better development of knowledge and infrastructure necessary to control this disease.

RECOMMENDATIONS

Healthcare workers in Nigeria need to be trained to develop a high index of suspicion for Lassa fever. It has been identified that the outbreak peak occurs mostly in the dry season so training should be conducted around mid-end of rainy season. Communities should be constantly engaged and sensitized to make sure that they understand the role rats play in the transmission of Lassa fever and how they can keep their homes and communities safe from rats. Social mobilisation and risk should be continuous and on-going in the high risk areas and community infection prevention and control should be a part of this.

We recommend a review/ possible redefinition of Lassa fever as a disease entity in the country. Lassa fever should now be considered in febrile patients in Nigeria and efforts should be intensified towards the development of a rapid point of care (POC) diagnostic test for Lassa fever as well as development and validation an algorithm for screening patients with fever to make it more sensitive in picking out suspect cases of Lassa fever.

Expanding the network of laboratories that can confirm diagnosis of Lassa fever should be made a high priority item. Infection prevention and control should be established as a quality standard for every healthcare facility in Nigeria. There should be improved documentation and dissemination of the outbreak response and management to enable lessons learnt to be well documented and have a wider reach.

This review has some limitations; the quality of the articles used in the review was poor and different articles/reports gave varying figures for the same outbreak so we used NCDC figures anytime they were available. Only articles and reports available online and in the databases, we searched were used for the review and this implies that we may have missed out on some articles that were available in other databases and in libraries and repositories that are not online. However, this review article has given some pointer to the direction Lassa fever outbreaks have gone over the years and also provides some insight into ways of looking at Lassa fever in Nigeria going forward.

REFERENCES

1. Eze KC, Salami TAT, Eze IC, Pogoson AE, Omordia N, Ugochukwu MO. High Lassa Fever activity in Northern part of Edo State , Nigeria: re-analysis of confirmatory test results. 2010;17(3):526.
2. Achinge GI, Kur JT, Gyoh SK. Lassa fever Outbreak in Makurdi , North Central Nigeria: What You Need To Know. 2013;7(5):426.
3. Nasir IA, Sani FM. Outbreaks , Pathogen Containment and Laboratory Investigations of Lassa fever in Nigeria: How Prepared Are We? 2015;10(1):110.
4. McCormick JB. Epidemiology and Control of Lassa Fever. 1987;134:6978.
5. Ibekwe TS, Okokhere PO, Asogun DA, Blackie FF, Nwegbu MM, Wahab KW, et al. Early-onset-sensorineural hearing loss in Lassa fever. Eur Arch Oto-Rhino-Laryngology. 2011;268(2):197201.
6. Ogbu O, Ajuluchukwu E, Uneke CJ. Lassa fever in West African sub-region: an overview. 2007;(March). 7. Tomori O, Fabiyi A, Sorungbe A, Smith A, Mccormick JB. viral hemorrhagic fever antibodies in Nigerian population. Am J Trop Med Hyg. 1988;38:40710.
8. Birmingham K, Kenyon G. Lassa fever is unheralded problem in West Africa. Nat Med. 2001;7:878878.
9. Frame JD. Lassa fever, a new virus disease of man from West Africa I. Clinical description and pathological findings. Am J Trop Hyg. 1970;19(4):6706.
10. WHO | Lassa fever. WHO. 2017;
11. Nissimov TB. Lassa fever: another threat from West Africa. Disaster Mil Med. 2016;
12. Richmond JK, Baglole DJ. Clinical review social consequences. 2002;12715.
13. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA

Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. 2009;6(7).
14. Monath TP. Lassa fever: review of epidemiology and epizootiology. 1975;52:57792.
15. Troup J, White HA, Fom A, Carey D. Outbreak of Lassa fever on the Jos plateau, Nigeria, in January-February 1970. Am J Trop Med Hyg. 1970;19:6956.
16. Carey DE, Kemp GE, Troup JM, White HA, Smith EA, Shope RE. Epidemiological aspects of the 1969 yellow fever epidemic in Nigeria. 1972;64551.
17. Bowen GS, Wulff H, Casals J, Noonan A, Downs WG. Lassa fever in Onitsha , East Central State , Nigeria , in 1974. 1975;52(Table 1):599604.
18. Ogoina D. Lassa fever: A clinical and epidemiological review. Niger Delta J Medicical Res. 2013;1(1):110.
19. Nasidi A, Fakile Y, Hutwagner L, Mccormick JB. Review ofcases of nosocomial Lassa fever in Nigeria: the high price of poor medical practice. 1995; 311: 19935.
20. JPRS Report. Epidemiology. 1993.
21. Nseir S, Roussel-delvallez M. Lassa Fever , Nigeria , 2003. 2005;11(10):16424.
22. Ehichioya D, Hass M, Olschlager S, Becker-ziaja B, Chukwu C, Coker J, et al. Lassa fever Nigeria 2005-2008. Emerg Infect Dis. 2010;16(6).
23. Adewuyi G, Fowotade A, Adewuyi B. Lassa fever: Another infectious menace. J Clin Exp Microbiol. 2009;9(1):14455.
24. Ilesanmi OS, Omotoso B, Alele FO, Adewuyi P, Centre FM, State O. Original Article Awareness of Lassa Fever in a Rural Community in South. 2015;4(1):110.
25. March J, Ajayi NA, Nwigwe CG, Azuogu BN, Onyire BN, Nwonwu EU, et al. International Journal of Infectious Diseases Containing a Lassa fever epidemic in a resource-limited setting: outbreak description and lessons learned from Abakaliki , Nigeria. 2013;17.
26. FMOH N. Weekly Epidemiology Report. Vol. 6, No.44. 2016.
27. NCDC. Situation Report Nigeria Centre for Disease Control (NCDC). 2016/2017 Lassa fever outbreak in Nigeria. 2017.
28. Bello OO, Akinajo OR, Odubamowo KH, Oluwasola TAO. Case Report Lassa Fever in Pregnancy: Report of 2 Cases Seen at the University College Hospital , Ibadan. 2016;2016:13.
29. NCDC. Situation Report, 2018 Lassa fever outbreak in Nigeria. Epi week 01. 2018.
30. Bond N, Schieffelin JS, Moses LM, Bennett AJ, Bausch DG. Short Report: A Historical Look at the First Reported Cases of Lassa Fever: IgG Antibodies 40 Years After Acute Infection. 2013;88(2):2414.
31. NCDC. Viral haemorrhagic fevers preparedness an response plan. 2017.
32. Asogun DA, Adomeh DI, Ehimuan J, Odia I, Hass M, Becker-ziaja B, et al. Molecular Diagnostics for Lassa Fever at Irrua Specialist Teaching Hospital , Nigeria: Lessons Learnt from Two Years of Laboratory Operation. 2012;6(9).
33. Fisher-Hoch S, Tomori O, Nasidi A, Perez-Oronoz G, Fakile Y, Hutwagner L, et al. Review of cases of nosocomial Lassa fever in Nigeria: the high price of medical practice. BMJ. 1995;311:8579.
34. Ijarotimi IT, Oladejo JA, Nasidi A, Jegede O. Lassa fever in the State Specialist Hospital Akure, Nigeria: Case report , Contact tracing and outcome of hospital contacts. 2016;3(1).
35. Inegbenebor U, Okosun J, Inegbenebor J. Prevention of Lassa fever in Nigeria. Trans R Soc Trop Med Hyg. 2010;104:514. 36. Okokhere PO, Ibekwe TS, Akpede GO. Journal of Medical Case Reports Sensorineural hearing loss in Lassa fever: two case reports Case presentation. 2009;3:13.
37. Fatiregun A, Isere E. Epidemic preparedness and management: A guide on Lassa fever outbreak preparedness plan. Niger Med J. 2017;58(1):16.
38. Iroezindu MO, Unigwe US, Okwara CC, Ozoh GA, Ndu AC, Ohanu ME, et al. Lessons learnt from the management of a case of Lassa fever and follow-up of nosocomial primary contacts in Nigeria during Ebola virus disease outbreak in West Africa. Trop Med Int Heal. 2015;20(11):142430.
39. Adebimpe W. Pre-epidemic preparedness and the control of Lassa fever in Southern Nigeria. Res J Heal Sci. 2016;4(3):24354.