Pattern and Outcome of Lassa Fever cases in Nasarawa State, Nigeria (2017-2022)

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Abstract

Background Lassa Fever (LF), an endemic zoonotic disease requires a 'One Health approach'.
Introduction A prior study in Nasarawa state (2013) showed a **high seroprevalence range of 10-25%, having a** serious impact on the health care system and families with significant socioeconomic losses to the state which necessitated this study
Methods This retrospective cross sectional study in Nasarawa State over five years (2017-2022) utilized all secondary data from all the Local Government Areas.
Results showed a Case Fatality Rate of 61% indicating high viral virulence, with the highest prevalence over the past 6 years in Keffi LGA. The trend analysis shows a fluctuating pattern of LF cases with 2 reported deaths of health workers (2021) indicating an evolving epidemiological pattern of the virus. With 38 LF positives out of 343 cases, high period prevalence of 11%, and increased number of 'suspected' and 'probable' cases, it shows sub-optimal quality of care or presence of other diseases that mimic LF and hence a need to review case definition.
Conclusion There is a need for increased in-country laboratory testing/diagnostic capacities and events-based surveillance.

Tendance et issue des cas de fièvre de Lassa dans l'État de Nasarawa, Nigéria (2017-2022)

Résumé
Contexte de l'étude : La fièvre de Lassa (FL), une maladie zoonotique endémique, nécessite une « approche One Health » (Approche d'une santé)
Introduction : Une étude antérieure dans l'État de Nasarawa (2013) a montré une fourchette de séroprévalence élevée de 10 à 25 %, ayant un impact sérieux sur le système de santé et les familles avec des pertes socio-économiques importantes pour l'État qui ont nécessité cette étude.
Méthode de l'étude : Cette étude transversale rétrospective dans l'État de Nasarawa sur cinq ans (2017-2022) a utilisé toutes les données secondaires de toutes les zones de gouvernement local.
Les résultats ont montré un taux de létalité de 61 %, indiquant une virulence virale élevée, avec la prévalence la plus élevée au cours des 6 dernières années dans la LGA de Keffi. L'analyse des tendances montre une tendance fluctuante des cas de FL avec 2 décès signalés d'agents de santé (2021), indiquant une évolution du schéma épidémiologique du virus. Avec 38 cas positifs pour la FL sur 343 cas, une prévalence périodique élevée de 11 % et un nombre accru de cas « suspects » et « probables », cela montre une qualité de soins sous-optimaux ou la présence d'autres maladies qui imitent la FL et donc la nécessité de revoir la définition du cas.
Conclusion : Il est nécessaire d'accroître les capacités de test/diagnostic des laboratoires nationaux et la surveillance basée sur les événements.
Mots-clés : Taux de létalité, une santé, fièvre de Lassa (FL)

INTRODUCTION

Lassa fever, a viral (RNA) hemorrhagic fever was first discovered in 1969, in Lassa, a village in Borno state, in Northern Nigeria. Through the decades, the epidemiology of the virus has evolved and is increasingly recognized to be endemic in many parts of West Africa, including Nigeria, Benin, Ghana, Mali and the Mano River region (Sierra Leone, Liberia and Guinea). In 2018, the Nigerian Centre for Disease Control and Prevention (NCDC) reported the largest ever number of cases in Nigeria, with over 600 confirmed cases and over 170 deaths (1). The increase is not thought to be due to any new virus strains, and may at least be partially explained by increasing surveillance capacity and laboratory testing. Historically, outbreaks occur during the dry season (November to April), however, in recent years, cases have also occurred during the rainy season (1).

Lassa fever (LF) is an epidemic prone disease for immediate notification on the Integrated Disease Surveillance and Response (IDSR) platform in Nigeria. The actual incidence rate in Nigeria is unknown, but case fatality rates range from 3% to 42% (and over the last two years has remained between 20% and 25%)(1).

Research Questions

- What is the pattern of Lassa fever over the years 2017-2022 in Nasarawa state?
- What has been the outcome of Lassa fever cases in Nasarawa state?

Objectives of this study

- To identify the trend of distribution of Lassa fever disease in Nasarawa state from 2017-2022
- To determine the Case Fatality Rate (CFR) over the years 2017-2022 and the overall average CFR for Nasarawa state
- To determine the average prevalence rate for Lassa fever in Nasarawa state

MATERIALS AND METHODS

Study Area

Nasarawa state is situated in the North Central geopolitical zone in Nigeria, within the latitude of 9.08'20" N and longitude of 8.19'97" E. It is bounded in the north by Kaduna state, in the west by the Federal Capital Territory, east by Taraba and Plateau states and Kogi and Benue states in the south. It has a total of 13 Local Government Areas (2) in which are a total of 1,035 public and private health facilities. Of these, 473 are public health facilities (450 primary healthcare centers (PHCs), 21 secondary and 2 tertiary health facilities). The tertiary hospitals- Dalhatu Araf Specialist Hospital and Federal Medical Centre Keffi (3) are the health facilities cases of Lassa fever are treated in, as the last point of referral within the state. Tertiary hospitals offer emergency care including the 'Intensive Care Unit', specialized medical and surgical departments with consultants in charge. Currently, the projected population using the 2006 census at a growth rate of 2.41%(4), is 2,793,169 people(5), majority of whom are farmers and businessmen.

Study Design

This was a retrospective cross sectional descriptive study in Nasarawa state from secondary data of tertiary health facilities.

Study Population

All 'suspected', 'probable' and 'confirmed' Lassa fever cases were included in the study for the period (2017-2022). Definitions according to the National Guidelines on Nigeria Lassa fever Case Management (6) are:

Suspected Lassa fever case: A patient with fever for 3-21 days with a measured temperature of 38 C or more with one or more of the following: vomiting, diarrhea, sore throat, myalgia (muscle pain), generalized body weakness, abnormal bleeding, abdominal pain. OR In Neonates: Maternal Lassa fever +/- signs and symptoms.

Any of the following scenarios should raise the index of suspicion:

a. Patient has not responded to standard anti-malaria treatment and

treatment for other common infectious causes of fever within 48-72 hours

b. History of recent contact with a probable or confirmed case of Lassa fever within 21 days of onset of fever

c. Patient with history of fever and history of travel to high risk/burden area of Lassa fever

d. Contact with body fluids or tissues of a dead patient with a febrile illness

Probable case: A suspected case who has one or more of the following complications- hearing loss, facial or neck swelling, seizures, restlessness, confusion, hypotension (SBP< 90mmHg in adults and <70mmHg in children), oliguria (<0.5ml/kg/h for 6 hours), abnormal bleeding

and any of the following supporting laboratory features. Laboratory features include

(i) proteinuria and/or microscopic hematuria (ii) Elevated urea ≥45 mg/dl or creatinine ≥2 mg

(iii) Elevated transaminases (liver enzymes, ALT

& AST) (iv) Reduced platelets count ≤90,000 cells/ml3. However, absence of the above listed complications and laboratory evidence does not rule out Lassa fever.
Confirmed case: A suspected or probable case with a positive laboratory test using real time polymerase chain reaction

Data Collection Technique

A quantitative data collection method using secondary data of tertiary health facilities was utilized. Data retrieved from the medical records department of the hospitals was collected, collated and entered into monthly reports submitted to the Nasarawa State Ministry of Health through the National Health Management Information System and IDSR.

Measurement of variables and data analysis

The variables of interest (outcome variables) include the 'Interval between onset of symptoms', 'time of admission (days)', 'Lassa fever test result', and 'outcome of illness'. Illness were measured/defined as self-reported ailments of Lassa fever warranting medical care or diagnosis given by a professional healthcare provider (medical doctors, nurses, laboratory scientists). Data were coded, entered, cleaned and analyzed by IBM Statistical Product and Service Solutions (SPSS) version 22.0 for Windows (SPSS, Chicago, Illinois, USA) and Excel 2010. Results were presented in text, tables and figures. The demographic variables were expressed in frequencies and percentages. Chi-square and fisher's exact were used to test associations and differences where appropriate. A p-value less than 0.001 was considered significant.

Ethical considerations: Ethical approval was obtained from the Research and Ethics Committee of the Nasarawa state Ministry of Health

RESULTS

Majority 99(28.9%) of the Lassa fever case participants were in the age range of 21- 30 years with a mean of 29 years, and 2.9% were >60 years. There was an almost equal distribution of male and female patients. Cases were seen in a total of 11 out of 13 Local Government Areas (LGAs). The 2 LGAs with no reported cases over the period 2017 – 2022 were Nasarawa and Toto. The highest number (56%) of cases were located in Keffi LGA followed by Lafia LGA (13%) and a low rate in Akwanga LGA (3%) Keana LGA (5%).

Out of the 190 patients with complete record of date of onset of symptoms and date of admission, majority 117(61.6%) had an interval from onset of symptoms and admission of between 0-4 days. Forty-four (23.2%) had between 5-9 days interval from onset of symptoms and admission. The proportion decreases with increase in days from onset of symptoms and admission as depicted in table 2.

Out of the 190 patients with complete record of date of onset of symptoms and date of admission, 189(99.5%) were in-patients and only 1(0.5%) was an out-patient.

The number of positive and negative cases according to years is presented in table 4 above. The result showed a fluctuating trend in the number of positive and negative cases across the years. The highest percentage (19.0%) of positive cases was recorded in 2017. This was followed by in 2019 (18.8%) while the least percentage of 5.4% was recorded in 2018.

The outcome of infected patients with respect to years is as presented in table 5 above. The result indicated a fluctuating trend in the proportion of dead over the years. It was found that all the 4(100.0%) infected cases in 2021 died. In 2022, 69.2% of the infected patients died. In 2017, 2018, the proportion of dead recorded were 58.3%, 66.7% respectively while the least proportion 16.7% of dead was in 2019.

The *Case Fatality Rate* is total number of deaths due to Lassa fever / number of confirmed cases of Lassa fever = 23/38 x 100 which is high at 61%.

Null Hypothesis: There is no significant difference in the number of infected cases and outcome over the years.
No statistical significant difference was observed in the proportions of positive and negative cases over the period, (p=0.094).

DISCUSSION

Lassa fever disease is a zoonotic disease caused by the Lassa virus, a member of Arenaviridae RNA family of viruses. The virus is transmitted to man by infected multi-mammate rats, the *mastomys natalensis* species complex which is the vector/reservoir host. Humans become infected from direct contact with the urine and faeces of the rat which contains the virus, through touching soiled objects, eating contaminated food, or exposure to open cuts or sores[6]. The disease is endemic in parts of West Africa including Sierra Leone, Liberia, Guinea, and Nigeria. Neighboring countries are at risk to the disease due to the presence of the animal vector lives throughout the region (7).

NCDC reported that in 2022 compared to the year before, there has been a rising incidence of Lassa fever in endemic parts of Nigeria –Ondo, Edo and Bauchi. Seventy-two (72%) of all confirmed Lassa fever cases were reported from these three states while 23% were reported from another 24 states. The number of suspected cases has increased compared to that reported for the same period in 2021. There are higher rates of disease in urban zones (1). In this study, cases of Lassa fever were seen in a total of 11 out of 13 Local Government Areas (LGAs) with the highest number (56%) of cases in Keffi LGA followed by Lafia LGA (13%). The 2 LGAs with no reported cases over the period 2017 – 2022 were Nasarawa and Toto. Majority 99(28.9%) of the Lassa fever case participants were in the age range of 21- 30 years with a mean of 29 years, and 2.9% were >60 years. There was an almost equal distribution of male and female patients. Prior to this study, similar findings were seen in a study in 2013 (8), where the ratio of the 398 participants were in the ratio (M: F) 1.8:1, the age group 10-19 had the highest seroprevalence of IgM and the LGAs with high seroprevalence (range of 10-25%) were Nasarawa, Keffi and Lafia. This study revealed a high period prevalence of 11% compared to the latter study of 18%.

The Lassa fever study of significant scope conducted in Nasarawa state in 2022 was supported by Coalition for Epidemic Preparedness and Innovations (CEPI) and NCDC. It was an in-depth epidemiological investigation of the cases to understand the possible source of infection and the extent of spread of the disease following the death of health care workers, findings of which initiated the development of a vaccine against the disease(9). The study protocol of a prospective multi-site, cohort study to estimate incidence of infection and disease due to Lassa fever virus in five West African countries (the Enable Lassa research programme) including Nigeria (3 sites) was released in March 2023, and we await the findings(10).

The incubation period ranges from 1-3 weeks. 80% of infected persons will be asymptomatic or will have mild symptoms, one in five people will develop severe disease. Out of the 190 patients with complete record of date of onset of symptoms and date of admission, majority 117(61.6%) had an interval from onset of symptoms and admission of between 0-4 days. The proportion decreases with increase in days from onset of symptoms and admission as depicted in table 2. It shows that increased training of health care workers in the communities is needed and could help faster detection of symptoms by case definition and speedy referrals to appropriate hospitals for specialized care and treatment.

The overall case fatality rate (CFR) is 1%. CFR can reach 15% or can be as high as 50% during outbreaks among hospitalized patients with severe symptoms (11,12). In this study in Nasarawa state, the case fatality rate was 61%. This indicates the increasingly severity of the disease reaching epidemic proportions (>50%) (8) and viral virulence or the presence of an inadequate healthcare system for treatment and supportive care of the cases. Most studies in the past in Nigeria have focused on the virological and clinical considerations of the disease. Even fewer studies have dwelt with the stigmatization and discrimination of cases of Lassa fever by health personnel that has had an impact on the prognosis of cases (13). Highest number of health care worker deaths were reported in 2021.

CONCLUSION

National Lassa fever multi-partner, multi-sectoral Technical Working Group (TWG) continues to coordinate the response activities at all levels. However, even though number of cases of Lassa fever cases have decreased in the last three years, as the population of Nasarawa continues to increase, it is important for communities to have increased awareness on prevention and control of Lassa fever through health promotion activities in an integrated One Health approach.

Conflict of Interest: There is no potential conflict of interest to this article.

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Table 1: Demographic characteristics of study participants

Demographic characteristics	Frequency (n=343)	Percentage
Age group		
=10	44	12.8
11-20	65	19.0
21-30	99	28.9
31-40	67	19.5
41-50	37	10.8
51-60	21	6.1
>60	10	2.9
Mean ± SD	28.73±15.71	
Gender		
Male	175	51.0
Female	168	49.0
Location/LGA		
Keffi	192	56.0
Karu	17	5.0
Doma	12	3.5
Awe	11	3.2
Kokona	11	3.2
Keana	5	1.5
Nassarawa Eggon	19	5.5
Obi	20	5.8
Akwanga	3	.9
Lafia	46	13.4
Wamba	7	2.0

Table 2: Interval between onset of symptoms and admission (days)

Interval in days	Number of clients (frequency)	Percentage
0-4	117	61.6
5-9	44	23.2
10-14	17	8.9
15-19	5	2.6
20-24	4	2.1
25-29	3	1.6
Total*	**190**	**100.0**

Table 3: Distribution of patients type of admission (with complete record of date of onset of symptoms) and date of admission

Patients	Frequency	Percentage
In patients	189	99.5
Out patients	1	.5
Total	190	100.0

Table 4: Trend analysis: Number of positive and negative cases according to years

Year	Total cases n (%)	Number positive n (%)	Number negative n (%)	? ^{2}	p-value
2017	63(18.4)	12(19.0)	51(81.0)	9.027	0.060
2018	56(16.3)	3(5.4)	53(94.6)		
2019	32(9.3)	6(18.8)	26(81.3)		
2021	36(10.5)	4(11.1)	32(88.9)		
2022	156(45.5)	13(8.3)	143(91.7)		
Total	343(100.0)	38(11.1)	305(88.9)		

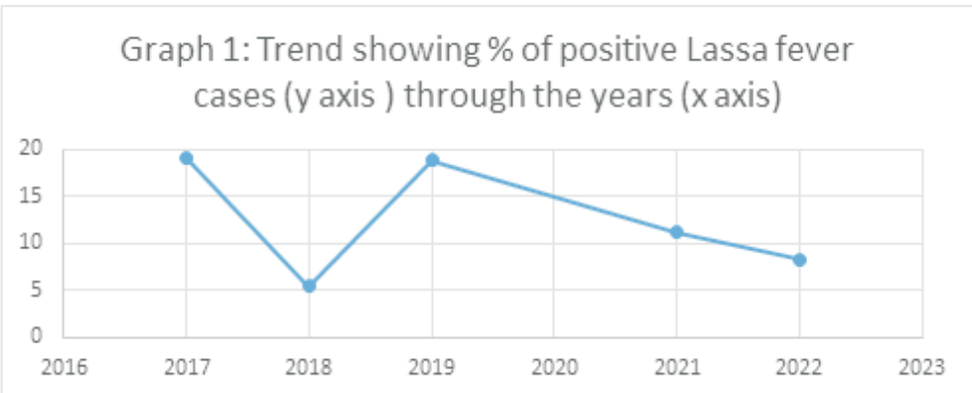

Table 5: Trend analysis: Number infected vs outcome over the years

Year	Total infected	Outcome		? ^{2}	p-value
	n (%)	Number Dead n (%)	Number Alive n (%)		
2017	12(31.6)	7(58.3)	5(41.7)	7.923	0.094
2018	3(7.9)	2(66.7)	1(33.3)		
2019	6(15.8)	1(16.7)	5(83.3)		
2021	4(10.2)	4(100.0)	0(0.0)		
2022	13(34.2)	9(69.2)	4(30.8)		
Total	38(100.0)	23(60.5)	15(39.5)