

EFFECTS OF COMORBIDITIES ON LASSA FEVER: A 5-YEAR RETROSPECTIVE ANALYSIS OF CASES ADMITTED IN A LASSA FEVER RESEARCH INSTITUTE IN NIGERIA (2019-2023)

ABSTRACT

Background

Co-morbidities in Lassa fever refers to the presence of other underlying medical conditions or diseases in individuals infected with the virus. These co-morbidities can significantly affect the progression and outcome of Lassa fever, making it a complex and challenging infectious disease to control.

Objective

To determine the effects of Co morbidities on Lassa fever and it's management between 2019-2023 in a Lassa Fever Research Institute in Nigeria.

Methodology:

This study was conducted at the Lassa Fever Research Institute at Irrua Specialist Teaching Hospital (ISTH) in Edo State, Nigeria. It engaged a retrospective cross-sectional design and employed a systematic sampling technique. Data analysis was done using IBM SPSS version 21.0 software for descriptive statistics. Associations were tested using the Chi-square test, with a significance level set at $p < 0.05$.

Results

The study found that Lassa fever had no specificity for age as it affected individuals across a wide age range (18-78 years), with the highest incidence in the 47-57 year age group. Hypertension was the most common comorbid condition (30%), followed by peptic ulcer disease (20%). Ribavirin was the main stay of treatment used. The analysis showed no significant relationship between comorbidities and mortality, as the majority of cases (85%) had outstanding outcomes. However, there was a significant relationship ($p=0.04$) between the level of education and outcomes, with most individuals having a tertiary education and experiencing positive outcomes.

Conclusion

According to this study, it was discovered that there were no significant relationship between co morbidities and mortality as majority of the cases reviewed were seen to have good outcomes with the aid of the current treatment (ribavirin).

Key word: Co-morbidities, Lassa fever, Lassa fever outcome, Lassa virus, Lassa Fever Outbreak, Hemorrhagic Fever

LIST OF ABBREVIATIONS

AIDS- *Acquired immune deficiency syndrome*

CDC- *Centers for Disease Control and Prevention*

HIV- *Human immunodeficiency virus*

LF – *Lassa fever*

PCR- *Polymerase chain reaction*

WHO - *World Health Organization*

UNDER PEER REVIEW

1.1 Introduction

Lassa fever, also known as Lassa Hemorrhagic Fever, is a viral illness that causes hemorrhagic symptoms. Although it was first recognized in the 1950s, the virus responsible for Lassa fever was not noticed till 1969 in a small town of Lassa in Northern Nigeria. [1]

It has been reported that up to 500,000 cases are handled which results in 5,000 deaths a year. Lassa high risk areas have been identified as the western and eastern extremes of West Africa. As of 2018, the Lassa belt covers Guinea, Nigeria, Sierra Leone and Liberia [2]. The mortality rate for those who make it to the hospital for the disease is about 15-20% [3].

The Lassa virus often transmits to humans from animals, particularly the natal **multiple breasted** mouse or African rat (*Mastomys natalensis*) [4]. It is the most common mouse in equatorial Africa, found in human households and eaten as a delicacy in some areas [5]. The mouse has the ability to produce a large number of children and colonize human settlements, increasing the risk of rodent-human contact, and is found in the west, central and eastern parts of the Africa [5]. When the mouse is a carrier, it passes out and spreads the virus throughout the rest of its lifetime through feces and urine creating more opportunities for disease to spread as they pass through grains and foodstuffs of resident humans [6]. The possibility of acquiring the infection through skin contact is relatively high as transmission from person to person has been established this poses a risk to health care workers [7]. The infective time lapse of Lassa fever ranges from 7–21 days after which it manifests wide spectrum of clinical symptoms which encompass headache, myalgia, fever, bleeding and seizures as well as encephalopathy and swelling of the face and neck [6]. In cases in which death occurs, this typically occurs within 14 days of onset. The risk of death is greater in women who are pregnant [8].

Lassa fever is not easy to easily differentiate it from other viral hemorrhagic fevers such as Ebola virus disease including other that cause fever, such as yellow fever, typhoid fever and malaria. The virus infections can only be made via the laboratory using the following tests: antibody enzyme-linked immunosorbent assay (ELISA), reverse transcriptase polymerase chain reaction (RT-PCR) assay, **and virus** isolation by cell culture, and antigen detection tests [9]. The antiviral medication ribavirin has been observed to show good enough promise [10].

Comorbidities associated with Lassa fever indicate the presence of other happenings of medical conditions present in individuals down with the virus. This can highly impact the outcome of Lassa fever, making it quite an infectious disease to manage. Hence, this study seeks to provide useful information that will help improve the quality of care in these patients and thus decrease the incidence of mortality associated with Lassa fever.

The impact of comorbidities on Lassa fever is significant, as even poor background health conditions can lead to morbidity and mortality. The dynamics of how these health conditions interplays with Lassa fever

is not yet fully understood. The economic burden of managing both comorbidities and Lassa fever is a major challenge. Therefore, the financial status of the patient directly affects the outcomes of those with comorbidities related to Lassa fever.

The health problems posed by the effect of the presence of comorbidities on the outcome of Lassa fever are overwhelming. Some of these comorbidities like HIV/AIDS, Diabetes mellitus, Sexually transmitted diseases and others tend to suppress the immune system of the patient thus providing comfortable grounds for the progression of Lassa fever in those affected.

Understanding how comorbidities interact with Lassa fever can significantly impact patient outcomes, treatment strategies, and clinical management. This knowledge can lead to improved care protocols and prompt investigation. Investigating comorbidities in Lassa fever helps in identifying populations at higher risk. This study will also contribute to public health strategies by providing data to create more effective prevention programs and awareness campaigns, especially for populations with prevalent comorbidities. The study targeted the following specific objectives: which include: determination of the prevalence of comorbidities in the disease condition, to ascertain the effect of co-morbidities on the clinical severity of Lassa fever and to determine the common co morbid conditions associated with Lassa fever.

2.0 METHODOLOGY

2.1 Study Design

This study was a retrospective cross-sectional study.

2.2 Study Area

This research study was conducted at Lassa Fever Research Institute in Nigeria of Irrua Specialist Teaching Hospital (ISTH) Edo State. The hospital has the following departments; Trauma & intensive care, Aged Care, Community Services, Diagnosis & Investigation, Medical & Surgical, Mental Health, Rehabilitation and Specialized Support Service. ISTH is also a Centre of Excellence in Teaching, Research and Service with particular reference to the health problems of rural and suburban/small urban town communities and the diagnosis, management and control of viral hemorrhagic fevers, with special reference to Lassa Fever. For the purpose of educating medical students and carrying out medical academic research, the state university - Ambrose Alli University is associated with this healthcare facility were Lassa fever, Ebola, and Covid-19 are other illnesses that it is well recognized for treating.

2.3 Study Population

The target **populations of the study were** the patients diagnosed with Lassa fever with known comorbidities, admitted to isolated wards between January 2019 and December 2023 in Irrua Specialist Teaching Hospital (ISTH) Edo State.

2.4 Study Duration

The study lasted for a period of 1 month

2.5 Inclusion Criteria

Patients admitted to isolation ward from January 2019 to December, 2023

2.6 Exclusion Criteria

Patient admitted to isolation ward that tested negative to the Lassa virus

2.7 Sampling technique

A systematic sampling technique was employed where the total number of cases notes within the month of January 2019 to December 2023. The first case note was retrieved randomly, and subsequent case notes were picked at an interval.

2.9 Data Management

2.9.1 Study Instrument

The instrument for data collection was drafted by the researchers. The checklist which comprised of 2 sections;

Section A: Socio demographic details

Section B: common comorbid conditions observed along with effect on management and co-morbidities associated with fatal cases of Lassa fever.

2.9.2 Data Collection method

Data will be extracted from the hospital health records/register of cases of Lassa fever with co-morbidities of patients admitted to isolated wards from January 2019 to December 2023 in Irrua Specialist Teaching Hospital (ISTH) Edo State. Information stored in the health facility's record will be utilized since they served as data for hospital management and as part of health information.

2.10 Data Analysis

Data was coded, entered and analyzed using Statistical Package for Social Sciences (SPSS version 25). Level of significance was set at $P < 0.05$. The outcome variables (on prevalence of Lassa fever and co-morbidities association) were analyzed using frequency distribution table.

3.0 RESULTS and DISCUSSION

This chapter deals with the analysis of collected data and presentation of results with the use of percentage, frequency tables and Charts. A total of 20 cases that fit into the study were reviewed over the duration of study.

TABLE 1: SOCIAL DEMOGRAPHIC CHARACTERISTICS OF PARTICIPANTS

VARIABLE	FREQUENCY N=20	PERCENTAGE
AGE IN YEARS		
18-27	4	20
28-37	4	20
38-47	2	10
48-57	5	25
58-67	2	10
68-77	2	10
>78	1	5
MEAN±S.D	43.75±18.59	
SEX		
Male	11	55.0
Female	9	45.0
OCCUPATION		
Business Man	1	5.0
Business Woman	1	5.0
Civil Servant	2	10.0
Farmer	1	5.0
Naval Officer	1	5.0
Nurse	1	5.0
Sales Manager	1	5.0
Security Officer	1	5.0
Student	1	5.0
Teacher	1	5.0
Trader	2	10.0
Nil Response	7	35.0

TRIBE

Esan	12	60.0
Etsako	3	15.0
Ibo	1	5.0
Igala	1	5.0
Owan	3	15.0

MARITAL STATUS

Single	4	20.0
Married	15	75.0
Widow	1	5.0

LEVEL OF EDUCATION

Primary	4	20.0
Secondary	1	5.0
Tertiary	10	50.0
Nil Response	5	25.0

From the above socio-demographic factors, it was observed that half of participants were between the age group of 48-57 years (50%) with a mean age of 43.75. There were more of males (55%) than females (45%), with civil servants and traders being the common among profession. Two-thirds were of the Esan speaking tribe. Majority (75%) of the case review were married with half of the cases having tertiary level of education.

TABLE 2: COMMOBIDITY

VARIABLE	FREQUENCY N=20	PERCENTAGE
Covid-19, Diabetics And		
Hypertension:	1	5.0
Diabetic:	3	15.0
Diabetics and Covid-19:	1	5.0
Hypertension:	6	30.0
Hypertension and Diabetics:	3	15.0
Peptic Ulcer:	4	20.0
Peptic Ulcer Disease And		
Hypertension:	1	5.0
Sickle Cell Disease:	1	5.0

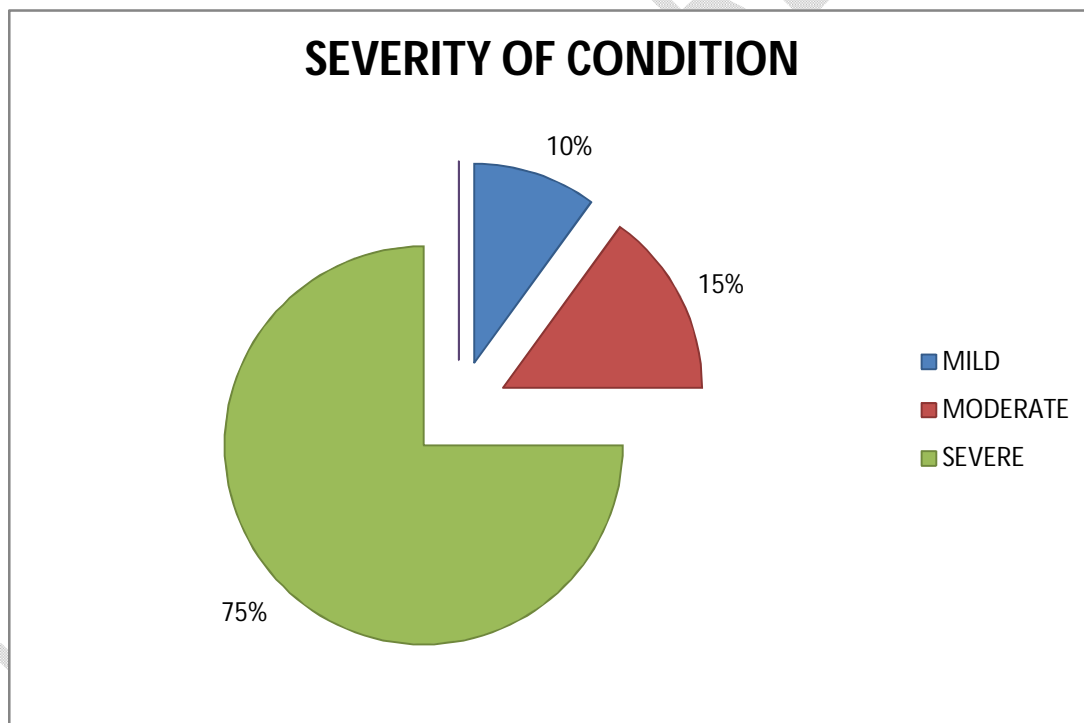


Fig 1: A Pie Chart Showing the distribution of severity of Condition

TABLE 3: DURATION OF ADMISSION STAY

VARIABLE	FREQUENCY	PERCENTAGE
N=20		
DAYS		
1-10	9	45
11-20	9	45
21-30	1	0.5
31-40	1	0.5

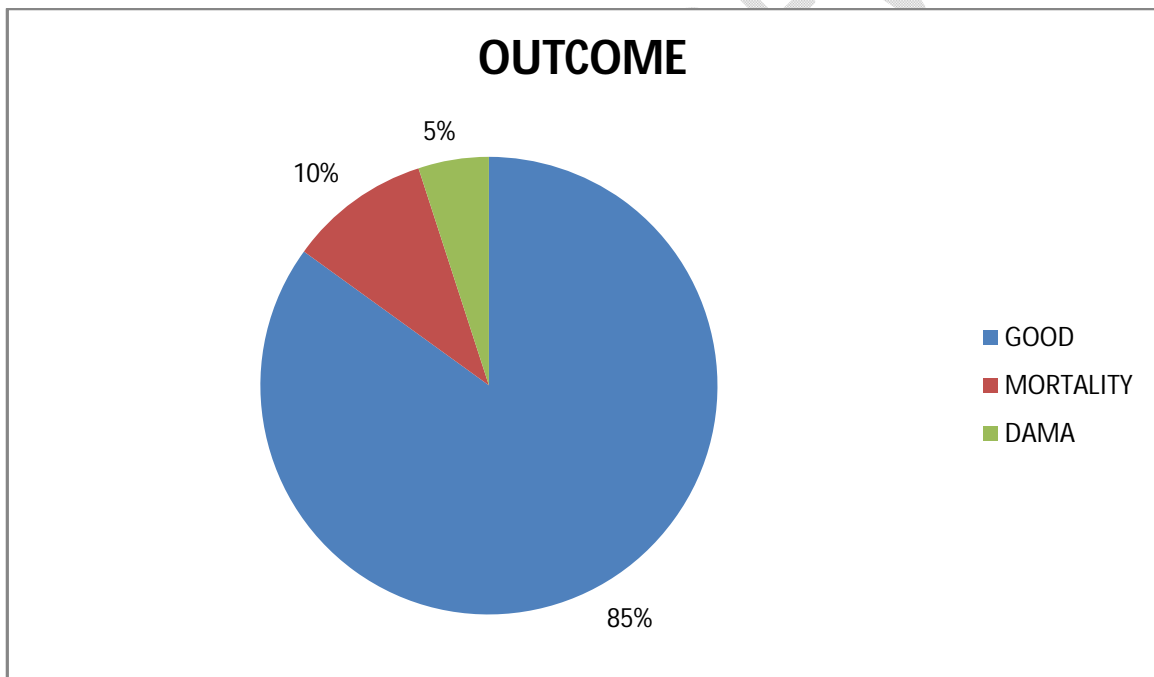


Fig 2: A Pie Chart Showing outcome

TABLE 4 ASSOCIATION BETWEEN SELECTED SOCIO-DEMOGRAPHIC DATA AND LEVEL OF OUTCOME.

SOCIO- DEMOGRAPHIC DATA	Variable OUTCOME LEVEL	TOTAL	χ²	P-val	
AGE IN YEARS	DAMA	GOOD	MORTALITY		
18-27	-	4 (20)	-	4 (20)	
28-37	-	4 (20)	-	4 (20)	
38-47	-	3 (15)	-	3 (15)	
48-57	-	3 (15)	1 (5)	4 (20)	
58-67	1 (5)	-	-	1 (5)	
68-77	-	1 (5)	-	1 (5)	
>78	-	-	-	-	
TOTAL	1 (5)	18 (90)	1 (5)	20 (100)	34.41 0.448
LEVEL OF EDUCATION					
Primary	0	4 (20)	0	4 (20)	
Secondary	0	1 (5)	0	1 (5)	
Tertiary	1 (5)	7 (35)	2 (10)	10 (50)	
Nil response	0	5 (25)	0	5 (25)	
Total	1 (5)	17 (85)	2 (10)	20 (100)	3.53 0.040*
OCCUPATION					
Business Man	0	1 (5)	0	1 (5)	
Business Woman	0	1 (5)	0	1 (5)	
Civil Servant	1 (5)	1 (5)	0	2 (10)	
Farmer	0	1 (5)	0	1 (5)	
Naval Officer	0	0	1 (5)	1 (5)	
Nurse	0	1 (5)	0	1 (5)	
Sales Manager	0	0	1 (5)	1 (5)	
Security Officer	0	1 (5)	0	1 (5)	
Student	0	1 (5)	0	1 (5)	
Teacher	0	1 (5)	0	1 (5)	
Trader	0	2 (10)	0	2 (10)	
Nil response	0	7 (35)	0	7 (35)	
Total	1 (5)	17 (85)	2 (10)	20 (100)	29.412 0.133

SEX

Male	0	9 (45)	2 (10)	11 (55)		
Female	1 (5)	8 (40)	0	9 (45)		
Total	1 (5)	17 (85)	2 (10)	20 (100)	2.888	2.36

There is a level of statistical significance found between level of education and the level of outcome where $P=0.04$ as the statistical level is set at $P<0.05$.

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TABLE 5 ASSOCIATIONS BETWEEN LEVEL OF SEVERITY AND LEVEL OF OUTCOME.

LEVEL OF SEVERITY	VARIABLE			TOTAL	χ^2	P _{val}
	OUTCOME LEVEL					
SEVERITY OF COMORBIDITY	DAMA	GOOD	MORTALITY			
Mild	0	2 (10)	0	2 (10)		
Moderate	0	3 (15)	0	3 (15)		
Severe	1 (5)	12 (60)	2 (10)	15 (70)		
Total	1 (5)	17 (85)	2 (10)	20 (100)	1.513	0.992

*Drug used in all treatment was Ribavirin.

The study focused on determination of the impact of Comorbidities on Lassa fever and its management between 2019-2023 in Lassa Fever research institute of Irrua Specialist Teaching Hospital.

In this study, the researchers were able to obtain access to the case notes for the period under review in order to thoroughly investigate the comorbidities and necessary outcomes that followed so as to present a vivid discussion on the current trend on ground thereby contributing to the bank of knowledge. In the process, the study researchers were able to find twenty (20) case notes that suited the study after thorough scrutiny of over 100 case notes for the study period under review. These were hence retrieved and further analyzed, noting the important details which included socio-demographic characteristics, comorbidity, severity of condition and outcome.

The fact that only 20 case notes were retrieved, given the few number indicates that there is a low prevalence rate of about 19%. This goes to point out that not many patients actually presents with comorbidities in addition to Lassa Fever.

From the Socio-demographic characteristics, it was observed that Lassa fever had at least an outcome from the young to the old as seen in the age group under review (18-78 years) with more presenting in the of 47-57 years. This was similar to a study done in Nigeria [11] where it was observed that middle and elderly age groups presented more with Lassa fever. In this study, males were majorly affected as seen in 55% of the cases notes compared to the female (45%) which was similar to the study done in Nigeria by Adebola et al [12]. The former study also reflected similar age group in cases of Lassa Fever. It was seen that the disease was more prevalent amongst the married people than single and those with tertiary level of education. There was no dominance in the level of infection among the occupation but in a study in Abakaliki [13], the condition was prevalent among traders. There was however no level of significant relationship between socio-demographic factors and comorbidities in the study.

It was seen that there was a level of statistical significance found between the level of education ($P=0.04$) and the level of outcome. This is due to the fact that majority of the participants had good outcome irrespective of their level of education.

Hypertension was observed to be the most prevalent comorbid condition (30%) which was closely followed by peptic ulcer disease (20%). However, it was observed that there were no significant relationship between comorbidities and mortality as majority of the cases reviewed were seen to have good outcomes. This was also in keeping with a study done in Nigeria in assessing the mortality of Lassa fever outbreak [11]. Ribavirin, a nucleoside analog, is the only drug with significant therapeutic benefit for patients when administered within 6 days of onset of illness, however highest duration of stay was seen between 1-20 days as seen in a study conducted in Plateau [14].

The study revealed good outcomes of recovery among patients as majority (85%) were seen to have recovered despite the severity of their presentation there was no significant association seen between outcome and severity of condition which was based on the state of clinical presentation. This was in contrast to the cases seen in Benin Republic [15] where about 30-40% mortality was recorded. In other studies by Okokhere et al [16] mortality was higher in patients with central nervous system involvement. In a similarity with a case study done in Enugu [17], it was seen that Lassa fever was independent of hypertension and diabetics as presented in a patient. However, due to the multi-presenting complaints such as fever, sore throat, made the condition very difficult to diagnose.

4.1 General public health implication of the study

Nigeria is presently experiencing LF outbreaks in some major cities, and LF may soon become a global concern if nothing is done to curtail the disease in the endemic regions. This is because it can be imported from endemic areas to other countries and it varies from season to season especially with the highest incidence reported during the dry season usually from November to early March.

Poor/inadequate knowledge and wrong preventive practices could aid the spread of infectious diseases among people. Poor epidemic preparedness has been indicated as one of the key factors contributing to disease outbreaks [18]. Therefore, it is necessary to investigate the level of awareness, knowledge, and prevention practices among the people about the disease, especially in the local communities where they are more prone to Lassa Fever because of the prevalence of rodents.

It is worth noting that self-medication can prolong illnesses, cause more complications, enhance spread to other people, make diseases more expensive to treat, lengthen hospital stays, and even result to death in some cases.

4.3 Conclusion

According to the findings in the study, it was discovered that the common Comorbidities associated with Lassa fever included; hypertension, peptic ulcer disease, diabetes mellitus and sickle cell disease. It was also discovered that there was a significant relationship between comorbidities and the severity of Lassa fever as 75% of cases had severe clinical symptoms although majority of the outcome was good.

4.2 Recommendations:

From our study, the following recommendations are made:

To the government/Legislators:

- a) More awareness on the Lassa Fever, prevention and control should be created employing all sources of social media, general public health promotion. This will help to educate those in the rural areas and reduce the spread of the disease.

- b) Government should organize training and retraining of health workers who will be at the fore front of curtailing the menace.
- c) More isolation and treatment centers should be created to enable and ensure proper control of the condition.
- d) There should be subsidization of Lassa fever treatment at little or no cost to encourage early presentation.
- e) Government should give more funds to the research of Lassa fever to speed up the process of production of drugs and possible vaccines used in management.
- f) Continuous collaboration with other affected countries, NGOs and foreign bodies to address the menace of Lassa Fever.
- g) Adequate laws should be made to curtail indiscriminate bush burning and hurting to help reduce incessant spread of the condition.

To the Public Health Physician/ and health workers.

- a) More awareness through seminars and medical outreach should be created for the on the menace of Lassa Fever.
- b) Proper handling of medical equipment and tools used in the management should be done with utmost concern and safety protocol.
- c) Health workers should dedicate their time into research in managing the condition better.
- d) Proper documentation should be done to keep on the current trend and control of the condition.
- e) High index of suspicion should be kept in mind when clinicians review cases of presentation similar to Lassa fever.

To the General Populace

- a) Suspected cases of Lassa Fever especially in endemic areas should immediately be reported to the nearest health center for prompt action.
- b) Early presentation is key and public who are well educated should keep this in mind.
- c) The public should also take time to go for regular health check and screening.

Ethical approval

Ethical approval for the study was sought from the research and ethics committee of Irrua Specialist Teaching Hospital. In order to ensure that the confidentiality the data collected, the names and addresses that were affiliated with the data collected were omitted.

Limitations of the Study

There sample size limitations and retrospective design should be noted. Future research directions would focus on longitudinal studies, expanded sample sizes across multiple centres and exploration of socioeconomic influences and genetic factors to enhance understanding and inform comprehensive public health strategies.

Also, at the time of conducting this study, most laboratory investigations such as information about viral load and severity of symptoms exhibited by the patients during the acute LF, and the profile of the

immune responses: antibody titers (total and neutralizing) and T cell responses were not within the reach of the researcher/authors. However, this noted observation has inspired the authors to put it into consideration in subsequent studies as it concerns Lassa fever

Disclaimer (Artificial intelligence)

Author(s) hereby declare and it should be duly noted that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts. This guarantees the fact that the originality of the study was maintained.

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