ORIGINAL RESEARCH

SPATIOTEMPORAL ANALYSIS OF LASSA FEVER CASES IN RIVERS STATE: IMPLICATIONS AND PREPAREDNESS

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Abstract

Background: Lassa fever (LF) caused by the Lassa virus (LASV) is a severe viral hemorrhagic fever endemic in some West African countries. It poses a tremendous public health challenge because of its high fatality rate and ability for outbreaks, the most common mode of rodent-human transmission occurs through direct touch, exposure, and infection of human meals with the excreta and also through contact with the blood and tissues of the infected multimammate rat. The study aims to assess and analyze the spatial distribution of Lassa fever cases in Rivers State from 2016-2022.

Methodology: The study utilized a retrospective descriptive study design. Cases of LF were extracted from records from the Department of Public Health, Rivers State Ministry of Health, showing the cases of LF in different years starting from 2015 to 2022 and at various locations. A Quantum Geographic Information System (QGIS) v3.83 was used to create a choropleth on the distribution of Lassa fever cases. The data were also analyzed using the SPSS v25 software at a 5% alpha level and were evaluated using the Chi-square test for categorical variables and the t-test for continuous variables.

Results: 73 suspected cases of LF were extracted from the record, 37 males and 36 females from which, most of the confirmed cases were females (7) and 6 males. The spatiotemporal analysis places Obio/Akpor Local Government Area as the high-risk area for LF in Rivers State, with the age group of at least 40 years having significantly increased likelihood of LF.

Conclusion: Lassa fever was found to be prevalent in densely populated areas, thereby making these areas hotspots for LASV. This could be associated with poor environmental management, indiscriminate disposal of refuse dumps, poor quality housing, and rural and urban migration. Therefore, there is a need for the government to activate strict environmental sanitation, effective risk communication, and the establishment of a robust surveillance team.

Keywords: Lassa fever, Lassa virus, Spatial, Spatiotemporal distribution, *Mastomys natalensis*

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INTRODUCTION

Lassa fever (LF) is a severe viral hemorrhagic fever found in humans. It is predominantly endemic in some West African countries like Nigeria. Lassa Fever is caused by the Lassa virus (LASV), an RNA virus that is a member of the *Arenaviridae* family.[1] The disease was first recorded in 1969 when a missionary nurse who was operating in Lassa town in Borno State died of it.[2]

Lassa fever is of significant public health concern in Nigeria. The disease poses a significant threat to human health because of its high fatality rate and ability to cause outbreaks. It imposes a great burden on affected communities and healthcare systems. Despite efforts to control and prevent Lassa fever, the burden of the disease remains high, which has necessitated various focused studies to address key problems.[3] The most common mode of rodent-human transmission occurs through direct touch, exposure, and infection of human meals with the excreta and also through contact with the blood and tissues of the infected multimammate rat. *Mastomys natalensis* is the natural reservoir of LASV which are rodents that live in and around human settlements.[4,5] The illness spectrum ranges from mild to very intense and sometimes fatal. Symptoms of Lassa fever arise within 1-4 weeks after getting in contact with the virus. The incubation period of this disease ranges from 2 days and sometimes extends to 21 days. The virus can be isolated within the blood, faeces, urine, throat swab, vomit, semen, and saliva of an infected person and secretion of the virus from infected individuals can continue for 30 days or more.[6] Poor knowledge about Lassa fever among the general population, healthcare workers, and key stakeholders hinders effective prevention and control measures. A well-timed and accurate diagnosis of Lassa fever is crucial for effective case management, prevention, and control.[7] However, diagnostic capabilities, particularly in resource-constrained settings, like Nigeria may be limited. The shortage of accessible and affordable diagnostic equipment, insufficient laboratory infrastructure, and inadequate training of healthcare experts contribute to delays in diagnosing cases and implementing appropriate interventions.[8,9]

Poor housing quality, personal hygiene, ineffective environmental sanitation, poor storage and preservative methods associated with post-harvest, and inadequate waste disposal and management in both rural and urban settlements have been shown to increase the population of the *mastomys natalensis* rodents in these settlements, thereby increasing the risk of the occurrence of LF infection. [10,11] Furthermore, the transmission of Lassa fever disease is directly associated with the concepts of spatial and spatial-temporal proximity and distribution. This, therefore, means that transmission of LASV is more likely to occur when the persons at risk are closely confined in a spatial and temporal space.[12] To comprehend the spread of the virus, it is imperative to understand that proximity to environmental risk factors is vital in the transmission of diseases. The temporal-spatial pattern of Lassa fever cases presents insights into the distribution and dynamics of the disease. Understanding these patterns is crucial for effective surveillance, prevention, and control strategies.[12]. The objective of this study is to assess and analyze the spatial distribution of Lassa fever cases in Rivers State from 2016-2022.

METHODOLOGY

Study design

The study employed a retrospective descriptive study design whose primary outcome is to describe and analyze the spatial distribution and the trend pattern of retrospective cases of Lassa fever in Rivers State, Nigeria.

Study Area

This study was carried out in Rivers State, which is a state in the Niger Delta region of the southern part of Nigeria. It is the 26th largest state in Nigeria by area size and the 6th most populous state with a population of about 5.2 million people as of the 2006 census, it is made up of 23 local government areas with the capital in Port-Harcourt. [14] Rivers State is predominantly a pluvial state, its inland part is made up of tropical rainforests, and towards the coast, it features mangrove swamps, it is bounded by the Atlantic Ocean and its topography consists of flat plains with a network of rivers. Rainfall is predominant and scarcely seasonal and occurs between March and November while the dry season is between December to February.[15] The economy of the state is dominated by the petroleum industries; however, the state is divided into urban and rural areas. While the urban areas are congested with industrialization, on the other hand, the rural areas which make up the greater population of the state are actively involved in farming as a major source of livelihood.[15] There are high human interchangeable movements from rural to urban areas, and vice versa. Therefore, making the state susceptible to the human-human transmission of the Lassa fever virus.

Case definition

Suspected case: A person presenting with fever (>38.0 °C) and one or more of the following symptoms: malaise, headache, sore throat, cough, nausea, vomiting, diarrhea, myalgia, chest pain, hearing loss, or any bleeding manifestation.[16]

Probable case: A patient who manifests all the classical symptoms of LF and has a clear history of contact with a confirmed case-patient but no laboratory confirmation.[16]

Confirmed case: A person with laboratory confirmation of Lassa virus infection, irrespective of clinical signs and symptoms. [16]

Study population

The study population comprises retrospective records of cases of LF in Rivers State extracted from the Department of Public Health, Rivers State Ministry of Health. The study included all suspected and confirmed cases of Lassa fever in Rivers State from 2016-2022. A total of 73 cases were obtained for this study.

Sampling Techniques

The geographic coordinates of LF case point locations were obtained using the geographic positioning system (GPS) and where locations could not be reached while using GPS, geographic coordinates were obtained using Google Earth Pro images for geo-positioning.

Maps of point locations, gender, and spatial distribution of Lassa fever cases were created and expanded for visualization.

Ethical Consideration

Ethical clearance was obtained from the Ethics and Research Committee of the School of Public Health, University of Port-Harcourt. Permission and authorization were also obtained from the Permanent Secretary through the Director of the Department of Public Health, Rivers State Ministry of Health.

Data Analysis

The summary statistics were presented using frequencies, percentages, tables, and graphs. Logistic regression was used to assess the association of gender and age groups with the occurrence of Lassa fever. All analysis was done using the SPSS v25 software at a 95% confidence interval and a p-value less than 0.05 was considered statistically significant. For the geospatial mapping and visualization of the environment, the geographic coordinate of the confirmed case point locations was obtained using a Quantum Geographic Information System (QGIS) v3.83 to create a choropleth on the distribution of Lassa fever cases in Rivers State, and the nearest neighbours index was also used to assess the spatial autocorrelation and spatial distribution of the confirmed Lassa fever and mortality cases.

RESULTS

A total of 73 cases of Lassa fever were analysed for this study

Table 1 shows the socio-demographic characteristics of Lassa fever cases. The age range of 30-39 years was higher for the cases of Lassa fever, (64.38%). With an average age of 35 years, the male gender also showed a higher value and the Lassa fever virus was predominant in the Obio/Akpor Local Government Area.

Figure I shows a comparison of the distribution and occurrence of Lassa fever from 2016 to 2022, and it indicated a higher distribution of occurrence in the year 2016.

Table 1: Demographics of suspected and confirmed cases

Variable	Unit	Frequency (n=73)	Percent (%)
Gender	Female	36	49.32
	Male	37	50.68
Age groups	<10	9	12.33
	10 – 19	3	4.11
	20 – 29	5	6.85
	30 – 39	47	64.38
	40 – 49	7	9.59
	60 and above	2	2.74
	Mean Age	35	
LGA	Obio/Akpor	62	84.93
	Degema	1	1.37
	Etche	4	5.48
	Ogu/Bolo	1	1.37
	Oyigbo	2	2.74
	Port Harcourt	3	4.11

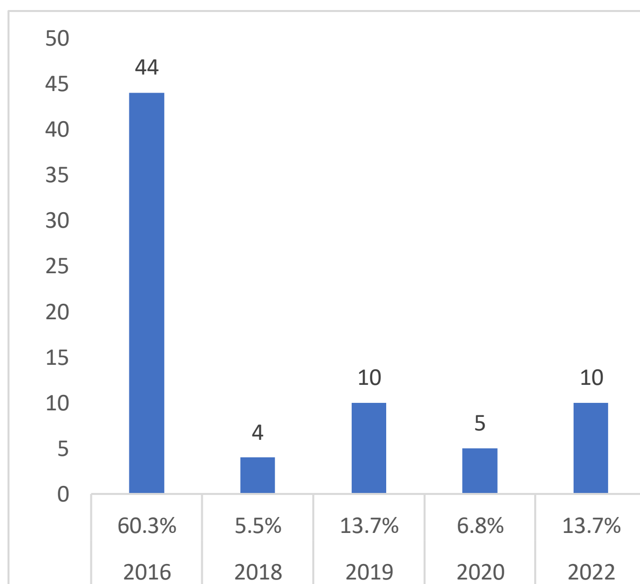


Figure 1: Distribution of cases of Lassa 2016 – 2022

Chi-square = 18.68,

Table 2: Association of Demographic Variables and Lassa Fever Positivity

		Lassa fever Status			
Demographic Variable	**Unit**	**Positive n(%)**	**Negative n(%)**	**Total n(%)**	**Chi-square (p-value)**
Gender	Female	7(19.4)	29(80.6)	**36(100.0)**	0.13 (0.719)
	Male	6(16.2)	31(83.8)	**37(100.0)**	
Age groups	<10	1(11.1)	8(88.9)	**9(100.0)**	
	10 – 19	0(0.0)	3(100.0)	**3(100.0)**	**13.07**
	20 – 29	2(40.0)	3(60.0)	**5(100.0)**	
	30 – 39	5(10.6)	42(89.4)	**47(100.0)**	**(0.023) ***
	40 – 49	4(57.1)	3(42.9)	**7(100.0)**	
	60 and above	1(50.0)	1(50.0)	**2(100.0)**	

**Distribution is statistically significant (p<0.05) p = 0.001 Distribution is statistically significant (p<0.05)*

Table 3 above shows that the occurrence of Lassa fever is not significantly associated with gender. However, the occurrence of Lassa fever was found to be significantly higher among persons aged 40 – 49 years (57.1%) in comparison to other age groups (chi-square = 13.07, p=0.023).

Table 3: **Distribution of confirmed cases by years**

	Lassa fever status		
Years	**Positive n(%)**	**Negative n(%)**	**Total n(%)**
2016	2(4.5)	42(95.5)	**44(100.0)**
2018	4(100.0)	0(0.0)	**4(100.0)**
2019	3(30.0)	7(70.0)	**10(100.0)**
2020	3(60.0)	2(40.0)	**5(100.0)**
2022	1(10.0)	9(90.0)	**10(100.0)**

Chi-square = 18.68
p = 0.001; Distribution is statistically significant

Table 4: Demographic distribution of outcome of confirmed positive cases

Variable	**Unit**	**Dead n(%)**	**Alive n(%)**	**Total n(%)**	**Chi-square (p-value)**
Gender	Female	5(71.4)	2(28.6)	**7(100.0)**	**1.88**
	Male	2(33.3)	4(66.7)	**6(100.0)**	**(0.170)**
Age groups	<10	1(100.0)	0(0.0)	**1(100.0)**	
	10 – 19	0 (0.0)	0 (0.0)	**0 (0.0)**	**5.75**
	20 – 29	2(100.0)	0(0.0)	**2(100.0)**	**(0.218)**
	30 – 39	4(80.0)	1(20.0)	**5(100.0)**	
	40 – 49	2(50.0)	2(50.0)	**4(100.0)**	
	≥60	1(100.0)	0(0.0)	**1(100.0)**	
LGA	Etche	1(100.0)	0(0.0)	**1(100.0)**	**2.02**
	Obio-Akpor	5(45.5)	6(54.5)	**11(100.0)**	**(0.363)**
	Oyigbo	1(100.0)	0(0.0)	**1(100.0)**	

Table 4 shows that none of the demographic variables (gender, age groups and LGA of residence) were significantly associated with mortality from Lassa fever.

Table 5: Demographic factors associated with Lassa fever from multivariate ordinal logistic regression

Demographic Variable	Unit	Lassa fever status Positive n(%)	Negative n(%)	Total n(%)	OR (95% C.I)	aOR (95% C.I)	p-value
Gender	Female	7(19.4)	29(80.6)	**36(100.0)**	*1.2 (0.3 – 4.1)*	*1.1 (0.2 – 4.4)*	0.718
	Male	6(16.2)	31(83.8)	**37(100.0)**			
Age groups	≥40 years	5(55.6)	4(44.4)	**9(100.0)**	*8.7 (1.9 – 39.5)*	*9.1 (1.8 – 19.3)*	0.002*
	<40 years	8(12.5)	56(87.5)	**64(100.0)**			

*O.R: odds ratio, aOR: Adjusted odds ratio, *statistically significant (p<0.05)*

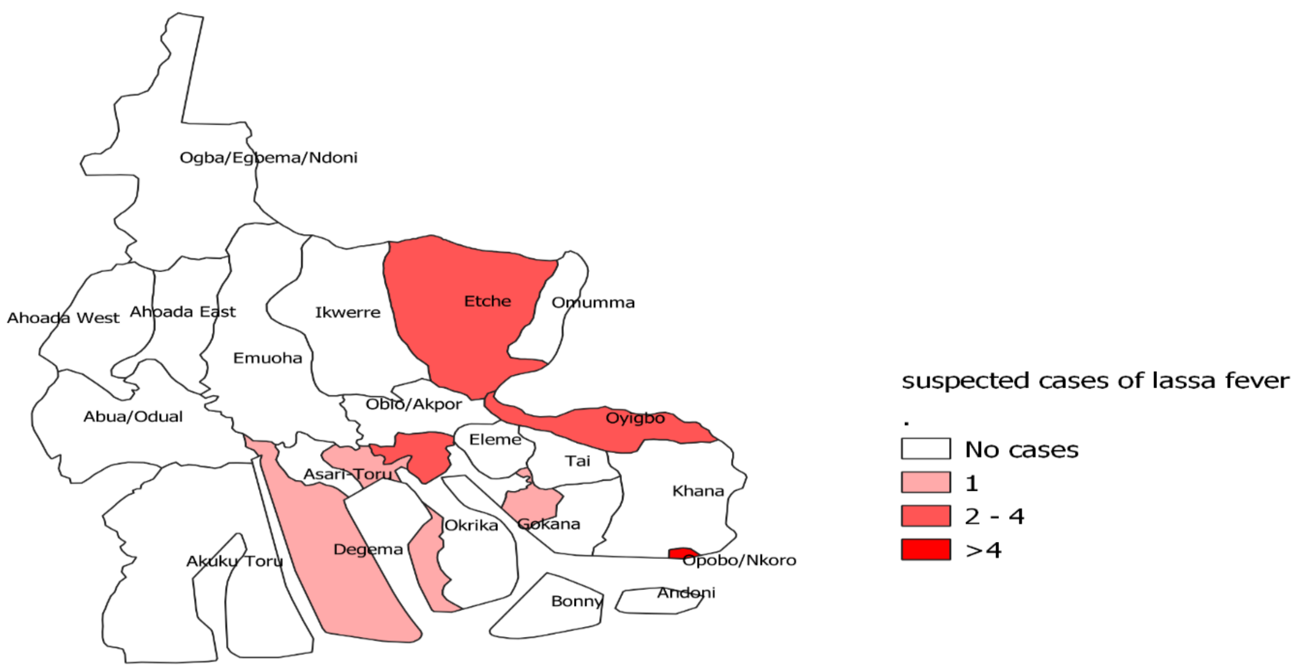
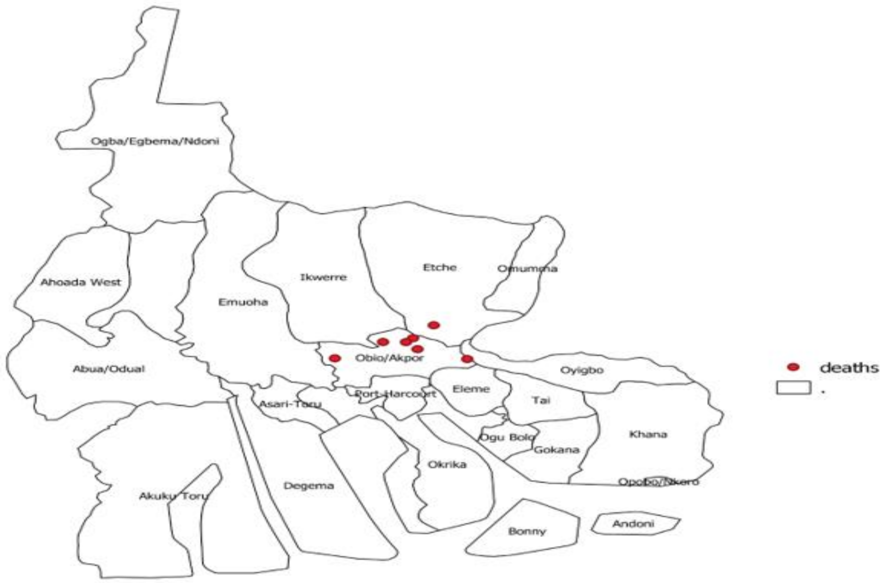


Figure 2: Distribution of suspected cases of Lassa fever among the Local Government Areas in Rivers State 2016 – 2022.

The table above shows that the females were 1.1 times more likely to have Lassa fever after adjusting for age group (aOR: 1.1; 0.2 – 4.4, p = 0.718). The table also shows that persons who were at least 40 years old were 9.1 times more likely to have Lassa fever after adjusting for gender (aOR:1.8; 1.8 – 19.3, p = 0.0002). In other words, the age group of at least 40 years significantly increases the likelihood of Lassa fever among the inhabitants.

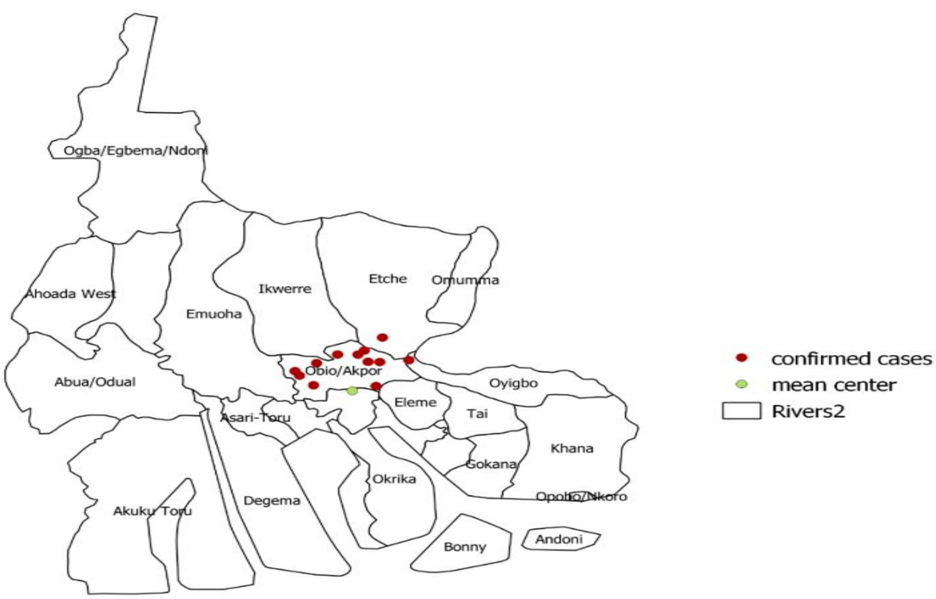


Nearest Neighbours Index (NNI) for Confirmed cases of Lassa Fever

Observed mean distance:0.0305692584686
Expected mean distance:0.0219069705714
Nearest neighbour index:1.39541240397
N:13
Z-Score:2.72742519409
p= 0.006391

Figure 3: Spatial distribution of confirmed cases of Lassa fever in Rivers State 2016 – 2022

The NNI of the confirmed cases is shown to be 1.39 with a p-value of 0.006, hence the distribution of the confirmed cases of Lassa in Rivers state is shown to be dispersed (evenly, distributed). (Note: when NNI = 1, distribution is random, NNI = 0, distribution is clustered, and NNI > 1, distribution is dispersed). The diagram shows that the mean center of the confirmed cases is in Port-Harcourt LGA.



Nearest Neighbours Index (NNI) for Lassa Fever Mortality in Rivers State

Observed mean distance: 0.04403170517854528,

Expected mean distance': 0.025090343902442996,

Nearest Neighbour Index': 1.754926331410627

N: 7,

'Z-score': 3.8210654482071624
P-value: 0.000133

Figure 4: **Spatial distribution of Lassa fever Mortality in Rivers State 2016 - 2022**

The NNI of the mortality from Lassa fever cases is shown to be 1.75 with a p-value of 0.0001, hence, the distribution of the mortality from Lassa fever in Rivers State is shown to be dispersed (evenly, distributed).
(Note: when NNI = 1, distribution is random, NNI = 0, distribution is clustered, and NNI > 1, distribution is dispersed).

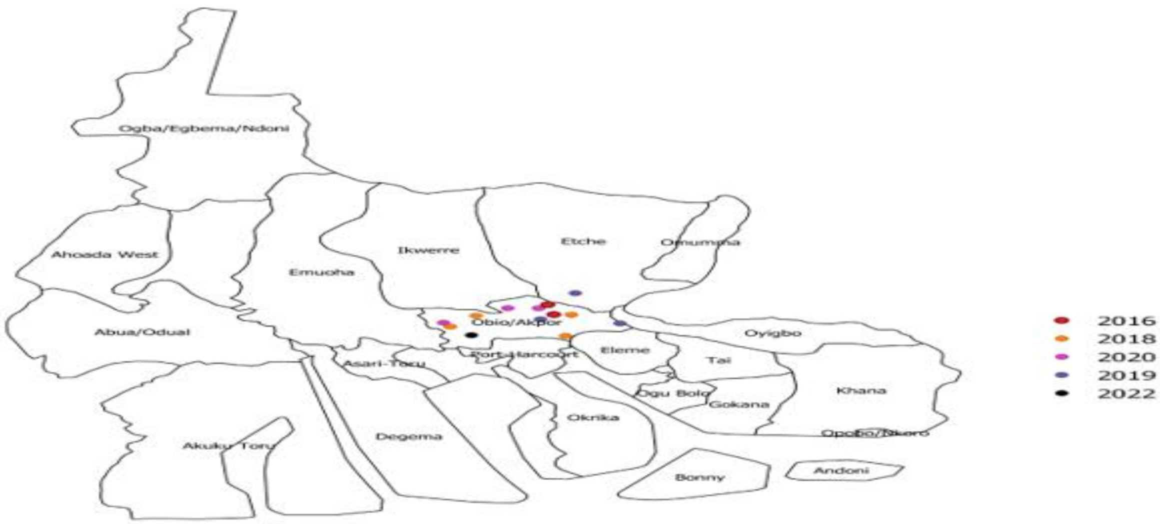


Figure 5: Temporal-spatial distribution of confirmed cases of Lassa fever in Rivers State

DISCUSSION

Lassa fever is an emerging and re-emerging disease with a potential for an outbreak.[17] The primary aim of the study is to analyze the spatial distribution of Lassa fever cases in Rivers State between 2015 and 2022. The socio-demographic representation of the Lassa fever cases from this study shows that the demographic variables of age and gender are not associated with the virus, however, the study revealed that the incidence of Lassa fever was found to be significantly higher among persons of older age. This collaborates with a study done by Ike, & Asogun,[18] that suggested that older citizens were susceptible to contracting the virus. This could be a result of a greater percentage of persons within this age range residing in clusters and hotspot locations of high-risk areas. The findings from this study also shows that most of the suspected cases of Lassa fever were male adults. This suggests that the mobility of the male population may also put them at risk of travel to high endemic states in Nigeria or at risk of making contact with the reservoir rodent vector, this observation conforms to a previous study.[19] However, despite the male adults being more on the suspected case distribution, the finding discovered that females accounted for a higher proportion of the confirmed cases of Lassa fever as compared to their male counterparts.[20] One of the factors that could be responsible for this rate could be the result of the domestic engagement of females in rural areas and socio-economic limitations burdened on them, and also the good health-seeking behaviour of the female gender gives them a fair chance of early diagnosis.[21]

The distribution of the confirmed cases of Lassa fever in Rivers State was dispersed in clusters. It was observed to be distributed in certain areas which are considered hotspot areas. These hotspot cluster areas are characterized by a higher incidence of Lassa fever cases compared to other regions in the state. Identifying and understanding the attributes of these hotspot areas is pertinent for effective disease control and prevention strategies. Some locations that are supposedly urban and metropolitan areas were indicated to be hotspots for Lassa fever. Interestingly, some schools of thought, perceived Lassa fever to be transmitted through rodents found mostly in rural areas,[5] and Lassa fever is commonly associated with rural settings. However, in contrast, some urban areas also experience sporadic cases suggesting that there is an increased movement from rural to urban areas which is a common practice in developing countries.[22] This increases the risk of transmitting the infectious virus from endemic high-risk rural areas to vulnerable urban locations and the potential of person-to-person spread. Urbanization can lead to increased interaction between humans and rodents especially in crowded living conditions or areas with poor sanitation infrastructure. Prompt detection, effective surveillance, and public health interventions are crucial in mitigating the risk of transmission in urban centers. The occurrence of a hotspot cluster indicates a higher level of disease transmission within that area. Factors that could contribute to this increased transmission may include a dense population, poor sanitation, and limited awareness about Lassa fever prevention measures.[23] This emphasizes that there is a monophyletic cluster at the village at a specific point in time and stationary circulation of the virus within a village and further virus exportation between villages.[24,25]The identification of the hotspot area may aid in the planning of public health interventions such as the distribution of resources. Identifying hotspot cluster areas also allows public health authorities to prioritize surveillance efforts. By closely monitoring these areas, health officials can detect new cases promptly, investigate potential sources of infection, and implement appropriate control measures to prevent further spread. [25]

The temporal-spatial distribution of the confirmed cases of Lassa from the study revealed that the distribution of Lassa fever cases was not uniform and displayed spatial variation. The disease tends to be more prevalent in certain areas compared to others. Plausible reasons adduced for this spatial distribution include proximity to rodent habitats, human population density, sanitation practices, and healthcare accessibility. The areas that recorded the highest number of dead cases of Lassa fever can be attributed to delay in seeking medical attention at the onset of the infection. Studies have shown that early detection and prompt treatment have proven useful measures in curbing the virus.[2,8,13] Other contributory factors could also be a result of low-quality housing, poor environmental sanitation, inadequate and indiscriminate waste disposal which has increased the population of the *Mastomys natalensis* rodents in these settlements, thereby increasing the risk of the occurrence of Lassa fever infection.[26] The interaction between humans and the environment plays a critical role in understanding the epidemiology of zoonotic viral diseases such as the Lassa fever virus, therefore there is a high risk of LF transmission in areas where human proximity to the environment such as farmers, hunters, etc, are closely associated with the rodent vector.[27] Death occurrence in rural areas may traced to the non-specific clinical manifestations due to lack of access to healthcare which causes delayed diagnosis and treatment.[4] *Mastomys natalensis* rodents most times find their way into households that have dirty and unkempt surroundings such as bushy compounds, open solid-waste dump sites, and disorganized domestic items. These rodents are usually attracted to waste dump sites that are exposed indiscriminately simply because they provide leftover food and a suitable environment for the rodent population to thrive, thus enhancing their breeding, and reproduction processes and have also been implicated in the transmission of the Lassa fever virus[28]. In Urban settlements and cities, due to the high cost of living, and inadequate housing, overcrowding in households is considered another environmental factor that makes people more vulnerable and at high risk of living with these vectors of Lassa fever. This finding is in accordance with previous studies,[25,29] which also stressed the fact that household proximity to high-risk areas such as rice mills, refuse dumps, storage facilities, and rice farms were some associated environmental factors that constitute a hotspot cluster area for LASV. In some parts of the study area, they experienced poor quality of housing, which is a requisite for rodent infestation,[10] suggesting that poor housing quality increases the risk of rodent infestation and Lassa fever, therefore, regular sanitation of the immediate environment and effective risk communication is key in curbing and controlling rodents and the spread of Lassa fever virus in the community.

CONCLUSIONS

Females are more likely to have an early detection of LF. The spatial distribution places Obio-Akpor and Port-Harcourt LGAs as hotspot areas of the LASV. The challenging effect of Lassa fever on the health systems of developing countries is a clarion call on the need to establish an effective surveillance and monitoring system for early detection while strengthening the preparedness of other preventive programs. By analyzing the temporal-spatial pattern and distribution of Lassa fever cases, public health authorities can develop tailored, targeted, and effective interventions to mitigate transmission and reduce the burden of the disease on the public.

RECOMMENDATIONS

There is a need for the government to establish healthcare facilities around the hotspot for early detection and diagnosis. The State Ministry of Health should engage the services of Disease Surveillance and Notification Officers, especially in rural areas where there is limited access to adequate laboratories in order to facilitate the immediate reporting of suspected cases of LF to designated public health surveillance offices. The government needs to activate strict environmental sanitation, effective risk communication, set up a robust surveillance mechanism, and strengthen global cooperation to establish preparedness protocols.

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