Contact Tracing and Profile of Lassa Fever Contacts in Edo State, Nigeria: Implications for the Control of Lassa Fever Outbreaks

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Abstract

Background: Edo State has recorded recurrent Lassa fever (LF) outbreaks in the past and had the highest proportion of confirmed cases in Nigeria in 2018. The aim of this study was to profile Lassa fever contacts and demonstrate the implications of contact tracing in the control of the disease.

Methods: This is a cross-sectional study which was based on secondary analysis of information derived from Lassa fever contact tracing forms used during the response to the LF outbreak of 2018 in Edo State. Contact tracing and data management were part of WHO's support to the State. Using SPSS, associations and other relationships between selected variables were tested. The significance level was set at $P<0.05$.

Results: Total contacts followed up were 2527 during the period under consideration. Higher mean contacts per case (CPC) was significantly associated with contacts in Edo South, with contacts of cases that died and with cases with symptomatic contacts ($F=8.307$, $P<0.001$; $t=14.995$, $P<0.001$; $t=6.161$, $P=0.014$ respectively). Following the integration of contact tracing with awareness campaigns, the number of newly diagnosed cases per week dropped from over 30 in the 7th week to 2 in the 13th week (42 days or 2 incubation periods).

Conclusion: Effective contact tracing contributed significantly to the identification of symptomatic contacts and to rapid control of the 2018 Lassa fever outbreak in Edo State. We recommend the deployment of effective contact tracing in the control of outbreaks of viral haemorrhagic fevers especially Lassa fever.

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Introduction

Lassa fever, a viral haemorrhagic fever (VHF), is transmitted primarily to man from rodents.[1]an Old World arenavirus (family Arenaviridae *Mastomys natalensis*, a multi-mammate peri-domestic rodent, is the main vector known to transmit the disease, while a few other species have been implicated.[1–3] Studies have indicated that rodent-to-human transmission as well as human-to-human transmission occurs in endemic communities and during outbreaks. In Nigeria, Lassa fever outbreaks have become almost a yearly occurrence. Edo State, a south-south state, recorded the highest number of cases in 2018.[4]

Response to Lassa fever outbreak included contact tracing, risk communication, promotion of infection prevention and control (IPC) practices, vector control and case management. Contact tracing is defined as the process of identification and follow-up of persons who may have come into contact with an infected person.[5] Contact tracing is applicable to viral haemorrhagic fevers such as Lassa fever and Ebola, HIV, and other sexually-transmitted diseases.[6–8] While there may be differences in the approach with respect to the specific disease and setting, the principles are basically the same- identifying exposed persons and preventing further spread of the infectious disease. In the case of Lassa fever (similar to Ebola), contact tracing involves contacts identification, contacts listing, contacts follow-up, and eventually contacts discharge after 21 days.[6, 9]

The essence of contact tracing is the early detection of secondary cases that may arise from exposure to primary (index) cases.[10] Early identification of symptomatic contacts helps to ensure quick laboratory testing. In the event that such symptomatic contact tests positive to Lassa fever, he or she is isolated early enough to prevent further spread of the infection. Contacts of Lassa fever cases are usually identified in the community (households and neighborhoods) and in the health care facilities where such cases were managed. In addition to typical (formal) health care facilities, Lassa fever cases may have received some care in drug vendors' shops, herbal healing homes and even faith-based centers. Contacts in transit (air, land and other means of travel) are difficult to track, especially where there are no readily available and properly documented manifests.[6, 11] This scenario is worse for intra-country land travel, especially in developing countries. There have been reported successes as well as challenges in contact-tracing air and land travel contacts of viral hemorrhagic fever (VHF) cases and other infectious diseases.[6, 12]

The geographic, demographic, and epidemiologic profile of Lassa fever contacts gives insight to the nature and distribution of the persons who have been exposed to cases of Lassa fever. An understanding of the profile of contacts of Lassa fever cases is thought to be helpful in designing effective contact tracing plan and efficiently deploying available resources to implement contact tracing in the context of overall outbreak response to disease outbreak. The aim of this research was to profile the contacts of Lassa fever cases and determine the implications of contact tracing during an outbreak of Lassa fever in Edo State, Nigeria.

Methods

This work adopted a secondary data analysis approach. Information from contact tracing formsroutinely entered into an excel data base was used for this study. The information was derived from the contact line lists and contact monitoring forms deployed by Lassa fever contact tracing supervisors and contact tracers engaged and coordinated by WHO Edo State Office during the outbreak of 2018 in Edo State. Edo State is located in the South-South geo-political zone of Nigeria.[13, 14] It is divided into 3 senatorial districts and there are 18 Local Government Areas (LGAs) in the state. The contact tracing teams were deployed in all LGAs in Edo State during the outbreak.

Information routinely obtained from Lassa fever contacts included demographic characteristics (such as age, gender, and location) and presence or absence of symptoms of Lassa fever. Contacts of Lassa fever cases were monitored for 21 days using the contact tracing forms. Blood samples for reverse transcriptase polymerase chain reaction (RT-PCR) tests were obtained by laboratory personnel from any contact found to have developed symptoms of Lassa fever during the contact tracing. The data from the excel sheets was exported to SPSS version 21 and cleaned.

The entire data base of contacts from January to July 2018 (covering a period of 6 months) was used for the analysis and summarized with proportions and means. Associations between locations of contacts and their demographic profiles were analyzed using Chi square. Similarly, relationships between the number of contacts per case (CPC) and some selected variables were tested using Analysis of Variance (ANOVA) and independent t-tests. The significance level was set at $P<0.05$. The database was stored in secured computers in the WHO State Office and the data used for this study was anonymized. Edo State Ministry of Health granted permission for the use of the Lassa fever data base for this research.

Results

Data sets for 2527 contacts of 200 cases of Lassa fever were analyzed.

The mean age of the subjects was 28.1±17.0 years, while the median age was 25 (15-38) years. Table 1 shows that majority of Lassa fever contacts were adults. There were more females than males and almost half of the contacts were in Edo central senatorial district. Over one-third of the subjects were health-facility contacts.

In Table 2, it is shown that most of the child and elderly contacts were community contacts and greater proportion of female contacts compared with male contacts had their contacts with Lassa fever cases in health facilities. In addition, Edo central district had the majority of contacts in the community. In all instances, the associations were statistically significant.

Figure 1 shows that 2.7% of Lassa contacts became symptomatic during contacts monitoring.

Figure 2 shows that 22.3% of symptomatic contacts turned out to be Lassa fever cases.

It is demonstrated in Figure 3 that there was a rapid decline of Lassa fever cases as well as recorded

Table 1: Demographic features of Lassa fever contacts

Variable	Frequency (N= 2527)	Percent
Age group		
Child (<18 years)	579	22.9
Adult (18-64 years)	1858	73.5
Elderly (≥65 years)	90	3.6
Sex		
Female	1591	63.0
Male	936	37.0
Senatorial districts		
Edo north	768	30.4
Edo central	1257	49.7
Edo south	502	19.9
Location of contact		
Community	1601	63.4
Health facility	926	36.6

Table 2: Association of the location of contacts with age, sex and senatorial district. Chi square analysis

Variable	Location of contacts		Statistics
	Community	Health facility	
	Frequency (%)	Frequency (%)	
Age			
Child	532 (91.9)	47 (8.1)	X^2=323.383
Adult	985 (53.0)	873 (47.0)	df=2
Elderly	84 (93.3)	6 (6.7)	P<0.001
Sex			
Female	886 (55.7)	705 (44.3)	X^2=108.772
Male	715 (76.4)	221 (23.6)	df=1; P<0.001
Senatorial district			
Edo north	424 (55.2)	344 (44.8)	X^2=221.877
Edo central	967 (76.9)	290 (23.1)	df=2
Edo south	210 (41.8)	292 (58.2)	P<0.001

deaths per week after the contact tracing together with sensitization, and active case search was commenced at the 7th epidemiological week. The number of newly diagnosed cases per week dropped from over 30 in the 7th week to 2 in the 13th week (42 days or 2 incubation periods).

Table 3 shows that more than half of Lassa fever cases had a small number of contacts, while only a small proportion had a large number of contacts. The majority of the cases did not have symptomatic contacts or Lassa PCR positive symptomatic contacts.

In Table 4, it is shown that Edo South had the highest mean number of contacts and Lassa fever patients who died had a greater mean number of contacts per case compared to those who survived. In both instances, the relationships were statistically significant. Similarly, the mean number of contacts per case was significantly associated with the occurrence of symptomatic contacts. However, PCR positive symptomatic contacts were not significantly related to the number of contacts per case.

Discussion

Adequate and appropriate response to Lassa fever outbreak is critical to containing the spread and minimizing associated morbidity and mortality of the

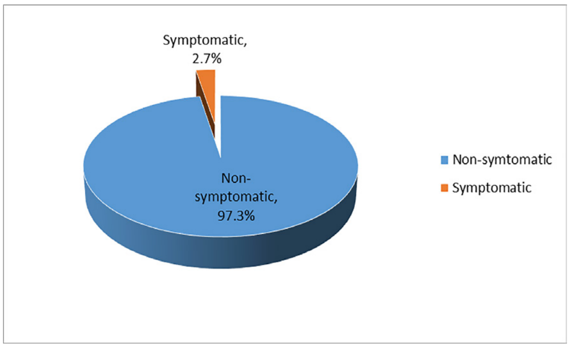

Figure 1: Overall distribution of symptomatic and non-symptomatic contacts (N=2527)

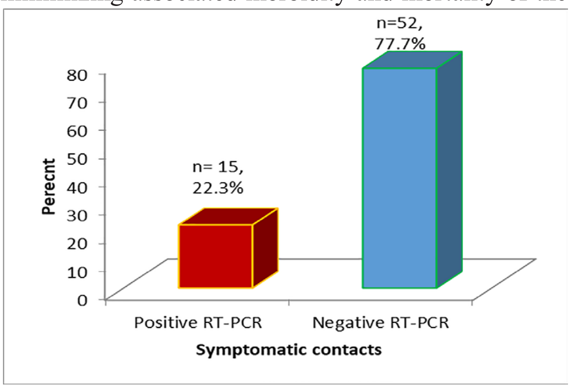

Figure 2: RT-PCR test results of symptomatic contacts (N=67)

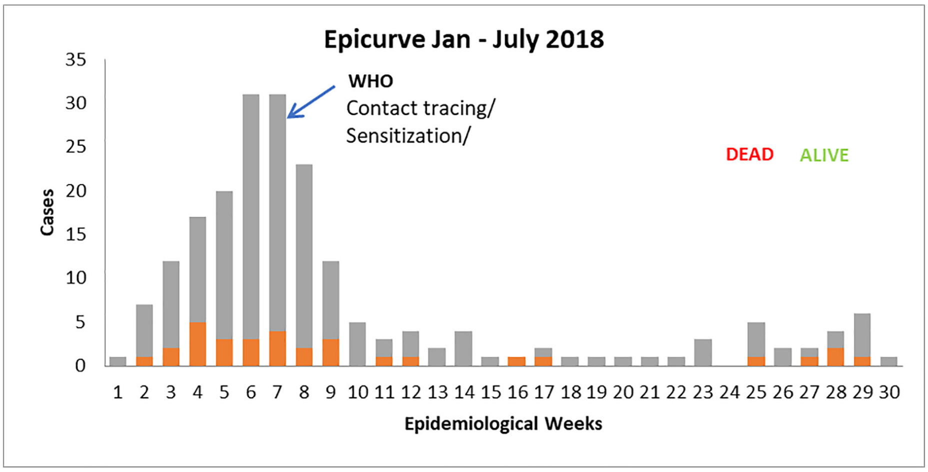

Figure 3: Declining cases and mortality after commencement of contact tracing together with sensitization and active case search

Table 3: Epidemiological features of the contacts of Lassa fever cases in Edo State

Feature	Frequency (N=200)	Percent
*Size of number of contacts per case (CPC)		
Small (1-9)	112	56.0
Moderate (10-49)	82	41.0
Large (50 or more)	6	3.0
Symptomatic contacts		
Yes	31	15.5
No	169	84.5
Lassa PCR positive symptomatic contacts		
Yes	11	5.5
No	189	94.5

*Mean CPC: 12.6±13.0

Table 4: Relationship between the number of contacts per case and selected variables. Analysis of variance and t-test

Variable	Mean	±Standard Deviation	Test Statistic	P value
Senatorial district				
Edo North	13.10	10.811	F=8.307	<0.001
Edo Central	10.78	12.595		
Edo South	23.67	17.191		
Case outcome				
Survived	11.13	11.808	t=14.995	<0.001
Died	20.53	16.144		
Cases with symptomatic contacts				
Yes	17.90	16.212	t=6.161	0.014
No	11.67	12.159		
Cases with PCR positive symptomatic contacts				
Yes	12.73	13.806	t=0.001	0.981
No	12.63	13.012		

disease. One important aspect of the response is contact tracing. Contact tracing is based on the epidemiological principles of transmission of communicable diseases.[1, 15, 16] Social networks cutting across households, communities and institutions (healthcare facilities) consisted of people who might have been susceptible to Lassa fever due to contacts with cases of the disease. More intimate contacts that increase the susceptibility to infectious disease occur in stable community settings than in transitory contacts.[17, 18]

In this study, there were more Lassa fever contacts in communities than in health facilities with nearly half of all contacts located in Edo central senatorial district. More contacts of Lassa fever are expectedly associated with increased number of Lassa fever cases. During the 2018 outbreak, the majority of cases were in the central senatorial district and this explains the larger distribution of contacts in the district.[19, 20]

Though majority of contacts were asymptomatic in this study, a near quarter of symptomatic contacts tested positive to Lassa RT-PCR. The large proportion of asymptomatic contacts observed in this study compares with the majority of asymptomatic contacts noted by Tambo and others.[21] In addition, the majority of symptomatic contacts and positive symptomatic contacts were found mostly in the LGAs with the highest burden during the outbreak. A missed contact who develop symptoms later on as a positive case contributes to onset of an outbreak as the (US) Centers for Disease Control and Prevention has noted in the case of Ebola.[9] A Nigerian study carried out in 2017 also reported how contact tracing contributed to the identification of suspected cases of Lassa fever and subsequent spread of the disease.[22]

Furthermore, contact tracing provided an opportunity to identify the suspected cases of Lassa fever in close contacts with confirmed cases even if they were cases of primary infection *ab initio*. Early detection of viral haemorrhagic fever cases and subsequent isolation and treatment are positive prognostic factors in survival.[7] Riding on the back of contact tracing, household and HCWs sensitization as well as active case search (ACS) in health care facilities, and in households and neighborhood of the reported cases were carried out by the teams following a concept the authors have captured as *contact tracing plus*. We believe that these activities (contact tracing, household and neighborhood sensitization and ACS) led to the significant reduction in the number of newly diagnosed Lassa fever cases per week from 30 to 2 new cases after 6 weeks (42 days) of commencement of the intervention. Contact tracing and sensitization activities are both important strategies in outbreak responses for Lassa fever and other VHFs.[7, 23]

The number of contacts per case (CPC) was highly varied, depicting the variation of factors that may affect the number and distribution of persons who were exposed to cases of Lassa fever. These factors may include the size and density of the social networks, duration of the onset of illness to isolation and the extent of intermediary care received (from peripheral health care and non-formal facilities) before definitive diagnosis was made and appropriate referral to treatment and isolation center was done.[17, 20, 24] This study sought to investigate the duration of time of onset of illness to commencement of treatment and the implications on disease outcome among patients. Data from case investigation forms (CIFs This study found significant associations between the CPC and the occurrence of symptomatic contacts and Lassa fever mortalities. An earlier study had demonstrated that reduced interval between the onset and presentation of patients at a Lassa treatment center had the potential to improve survival.[20]

One strength of this study was the demonstration of the usefulness of contact tracing in rapid identification of symptomatic contacts of Lassa fever and its use as a rationale for testing for the infection. There was no available data to determine if all positive symptomatic contacts were cases of secondary infection. This was a major limitation of this study. However, it is reasonable to assume that some of them may have been infected by coming in contact with index cases. A genomic sequencing analysis[25, 26] would have helped to trace the origins of Lassa infection in contacts of Lassa fever patients, but such an analysis was not within the scope of this research.

Conclusion

In conclusion, contacts of Lassa fever cases in this study were tilted towards general community members than health care facilities staff with highly varied number of contacts per case (CPC). Contact tracing provides an effective means to carry out other related outbreak response activities. We recommend the deployment of effective contact tracing in the control of outbreaks of viral hemorrhagic fevers, especially Lassa fever.

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