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ORIGINAL ARTICLE

Exposure Incidents and Outcome of Lassa Fever Virus (LASV) Infection among Healthcare Workers in Nigeria, 2019

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Abstract

Background: Lassa fever (LF) is a zoonotic disease endemic in Nigeria. Primary infection through exposure to excreta, urine or saliva of infected rodents is the most common mode of infection. There is documented evidence of human to human (HTH) transmission, especially among healthcare workers (HCWs) who are more at risk of nosocomial transmission in a hospital environment. In the 2018 Lassa fever outbreak in Nigeria, eight percent of all cases occurred among HCWs. This paper describes the patterns of exposure, characteristics and outcome of HCWs to Lassa virus (LASV) infection during the 2019 outbreak.

Methods: We analysed secondary demographic, epidemiological and clinical data extracted using a standardized questionnaire. Data was from infected HCW case notes, admission and discharge registers. Descriptive analysis of the collated data was performed using Microsoft Excel. Key findings were summarised in tables and figures.

Results: Nineteen HCWs were investigated out of which 17 (89.5) had exposure to a Lassa fever patient through provision of either medical/nursing, surgical care or laboratory supportive procedures. Two HCWs had needlestick injuries and another two had blood splash, as exposure incidents. Fourteen (73.7%) never had any form of general infection prevention and control (IPC) or Lassa fever specific personal protective equipment (PPE) training. Overall, compliance with IPC practice, especially with the use of PPE and other components of standard/transmission-based precautions was low and suggested to be potential contributing factors to HCW infections.

Conclusion: These exposure incidents suggest the need to constantly sensitise HCWs who work in Lassa fever treatment centres on routine practice of standard and transmission-based precautions when handling patients especially with febrile illnesses. This should include pre-employment and on the job trainings for HCWs on general IPC measures to observe and practice in the hospital environment.

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Keywords

Lassa virus (LASV) infection, Lassa fever, Healthcare workers, Nigeria

Introduction

Lassa fever (LF) is a viral hemorrhagic disease caused by Lassa virus (LASV) belonging to the arenavirus family [1]. Primary infection is by exposure to the excreta, urine or saliva of infected multimammate rodents. LF results in death of approximately 15%-20% of cases [2]. However, secondary human-to-human (HTH) transmission is possible and can occur via direct contact with the blood or body, therefore body fluids of infected patients are a risk to health care workers (HCWs) caring for Lassa fever cases [3,4]. Nosocomial infection with LASV is common among health care workers (HCWs) who manage Lassa fever cases, and this has been attributed to the lack of strict adherence to infection prevention and control (IPC) practices, including lack of use, inappropriate use, non-adherence or partial use of personal protective equipment (PPE) during the provision of care to infected patients [5]. Nosocomial transmissions are usually due to poor pathogen containment via lack of barrier nursing, ineffective sterilization, needle pricks and direct contact with infected blood and blood products during clinical procedures [5]. The risk of HCWs contracting the disease has continued to increase since the first reported nosocomial case in Lassa town, North-eastern Nigeria, in January 1969 [6]. Studies have shown that most cases of Lassa fever result from zoonotic spread among human populations, with clusters of suspected nosocomial transmissions reported within health care settings [4]. Evidence has also demonstrated high prevalence of antibody to Lassa virus among HCWs in locations where there had been a current or recent outbreak of the disease [7]. In some cases, the illness may result in some complications which include hearing loss, tremors and encephalitis [8]. Although, overall case fatality rate (CFR) is 1%, observed CFR among patients hospitalised with severe cases of Lassa fever is 15% [9]. Other studies have shown CFR as high as 31.6% among confirmed HCW cases [9,10]. There is an increased occurrence of Lassa fever in Nigeria given its endemic nature, further increasing the possibility of HTH transmission, and putting HCWs at constant risk of exposure to the virus [10-12]. The 2018 Lassa fever outbreak, being the largest among others in Nigeria was a major one. It was characterised by high morbidity and mortality among HCWs in tertiary health facilities as 37 (8.7%) of 423 confirmed cases were all HCWs among whom eight deaths occurred (CFR = 21.6). Sixteen of the 37 HCWS were reported from tertiary health facility in Nigeria [13]. Although heightened IPC strategies aimed at curbing the recurrence of these infections were instituted by the Nigeria Centre for Disease Control (NCDC), it is important to investigate the pattern and factors associated with LASV infection among HCWs in the 2019 outbreak given the high number of HCWs infected in the previous year's outbreak. This article describes the pattern of exposures, clinical features and outcome of LASV infections among HCWs in the 2019 outbreak.

Methods

Study design

This was a descriptive study on all HCWs who were infected and presented at the designated treatment centres during weeks 1-52, of the 2019 outbreak. A retrospective analysis of clinical records, surveillance and laboratory data was done using a tool developed by NCDC to collate the extracted data.

Study area

Nigeria is made up of 36 states and a Federal Capital Territory. There are 21 NCDC-designated treatment centres within tertiary health facilities in Nigeria. This study covers all States in Nigeria that reported at least one HCW LASV laboratory confirmed infection. Rapid Response Teams (RRT) from NCDC - who were constituted and deployed to various states and treatment centres at the beginning of the outbreak to support outbreak investigation and response - in collaboration with treatment centres case managers extracted the required data on all HCWs infections who presented at the designated treatment centres during the outbreak period, from the various record sources.

Case definition

For the purpose of this study we defined HCW infection as LASV infection confirmed by reverse transcriptase polymerase chain reaction (RT-PCR) in any HCW who got infected during delivery of health services to a suspected or confirmed Lassa fever patient. Lassa fever cases were defined using the National Guidelines for Lassa Fever Case Management [14]; in which a confirmed Lassa fever case is any individual presenting with one or more of the following:

Malaise, fever, headache, sore throat, cough, nausea, vomiting, diarrhea, myalgia, chest pain, hearing loss and either: (a) History of contact with rodents; (b) History of contact with a probable or confirmed Lassa fever case within a period of 21 days of onset of symptoms or any person with inexplicable bleeding/hemorrhage with RT-PCR laboratory confirmation.

Data source

We extracted and collated data from routine outbreak data sources such as completed Case Investigation case notes, laboratory, nursing records and discharge registers. As part of routine surveillance in Nigeria, all suspected cases have case investigation forms completed for them and blood samples are collected and tested using PCR [15]. Data extracted were pre-

Table 1: Demographic Characteristics of HCWS with LASV infection in Nigeria, 2019 (N = 19).

Characteristics	Number (Deaths)	Percentage (%)
Female	10 (2)	52.6
Male	9 (0)	47.4
Age groups (Years)		
Median	38	
Range	22-61 years	
21-30 yrs	5	26.3
31-40 yrs	6	31.6
41-50 yrs	6	31.6
51-60 yrs	1	5.3
> 60 yrs	1	5.3
Category of HCWs		
Auxiliary Nurse	3 (1)	15.8
Community Health Extension Worker (CHEW)	1 (0)	5.3
Doctor	9 (0)	47.4
Nurse	3 (1)	15.8
Medical Laboratory Scientist	2 (0)	10.5
Radiology Technician	1 (0)	5.3

senting symptoms/signs, possible exposure risks, types of procedures/care performed on positive Lassa fever patients, use/adherence to PPE and potential elements of community exposure/contact within the three-week period that preceded their symptoms.

Data management

All collected data was entered into an excel sheet. Descriptive analysis (demographics, clinical features and outcome) of the collated data was performed using Microsoft Excel and summarised (Table 1). This is presented as frequencies and percentages.

Ethical considerations

All the information extracted was as part of routine response data and activities. All data was kept confidential. Personal identifiers were not extracted and therefore not included in analysis. The data was safely stored in password embedded computers. A waiver for publication was sought from National Health Research Ethics Committee (NHREC).

Results

During the 2019 outbreak, 833 confirmed cases were recorded with 174 deaths (CFR = 20.9%). Of these confirmed cases, 19 (2.3%) were among HCWs and fully investigated. Table 1 shows the sociodemographic distribution of the HCWs.

The overall median age among infected HCWs was 38 years (range 22-61) with slightly more female HCWs (52.6%) affected. Nine (47.4%) doctors were affected, followed by nurses and auxiliary nurses with three cases each (15.8%), two laboratory scientists and one radiology technician. Table 2 shows the number of cases reported across the States. Edo and Ondo States having the highest numbers, each had five (26.3%) HCWs infected, followed by Ebonyi with 2 (10.5%) HCWs with the remainder of the states having one infected HCW each. Fourteen (73.7%) of the HCW infections occurred in a public health facility, while the remaining 5 (26.3%) were in private health facilities. Mortality recorded was 2 (10.5%), one each in Edo and Enugu States out of the 174 (CFR = 20.9%) total deaths in 2019 outbreak.

Table 2: Distribution of HCW Lassa fever cases by States (N = 19).

States	Number of Cases	Number of HCW Deaths
Bauchi	1	0
Benue	1	0
Delta	1	0
Ebonyi	2	0
Edo	5	1
Enugu	1	1
Ondo	5	0
Plateau	1	0
Rivers	1	0
Kebbi	1	0
Total	**19**	**2**

Presenting symptoms/signs

The common presenting symptoms were fever (73.7%), general weakness (36.8%), headache & vomiting (26.3%) each and cough (21.1%). None of the HCWs presented with a history of bleeding from body sites or any orifice. Two HCWs had had dark colored urine as presenting symptoms. Other infrequent symptoms presented by HCWs included epigastric pain, diarrhoea and conjunctivitis (Figure 1). Duration from onset of symptoms to when the HCWs first sought medical attention, ranged from 0-23 days with a median of nine days. During that period, 12 (63.2%) of the HCWs suspected they had malaria, while two (10.5%) suspected they had Upper Respiratory Tract Infections (URTI) and were treated with anti-malarial and antibiotic drugs, respectively. Eight out of the 10 HCWs who sought malaria treatment carried out self-medication and never reported to any medical facility during the period. Similarly, duration from onset of symptoms to commencement of IV Ribavirin for HCWs ranged from 4-33 days with a median of 11 days.

Pattern and types of exposure incidents

Out of the 19 HCWs, 17 (89.5%) had provided care to Lassa fever patients in isolation units, within 21 days of onset of symptoms while two did not provide any direct care to a confirmed Lassa fever patient. General medical/nursing non-invasive care (changing of bed lin-

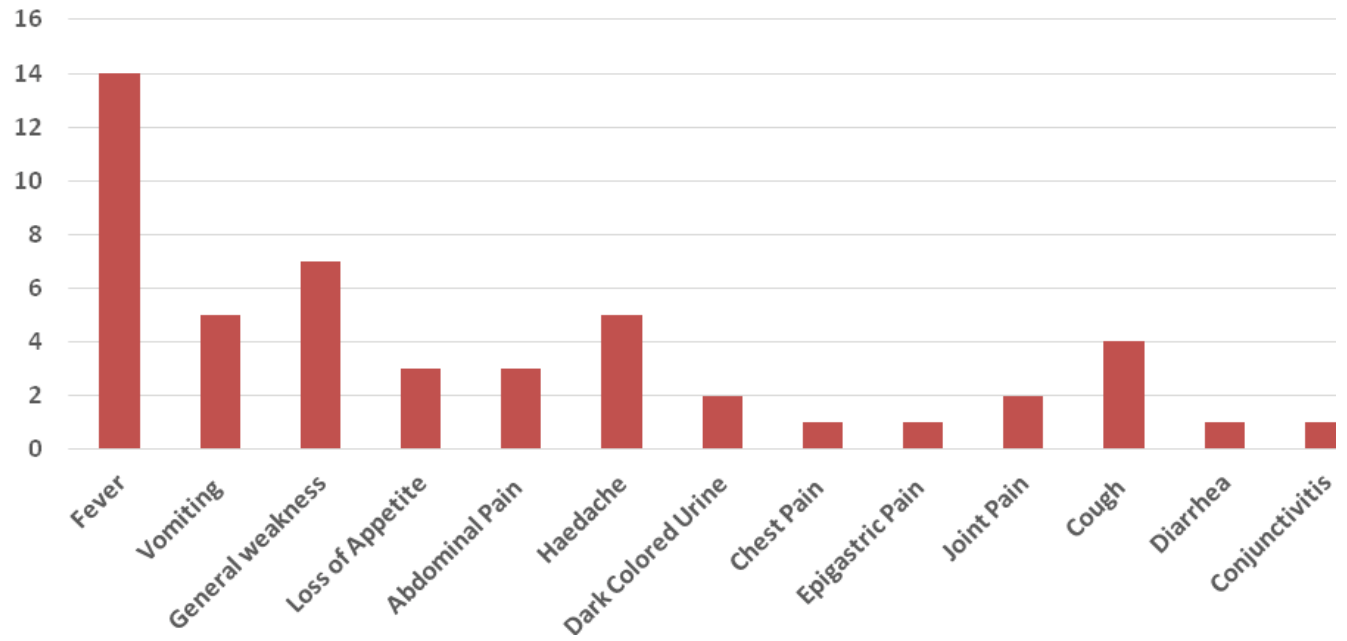

Figure 1: Distribution of symptoms among Lassa fever confirmed HCWs (N = 19*).
*No LF confirmed HCW had bleeding from any orifice (body site).

en, vital sign measurements, IV drug administration and emptying of urine bag) was provided to Lassa fever patients by seven HCWs. Surgical care like repeated venipuncture and catheterization were specific procedures provided by six HCWs. Two of the six HCWs who provided venipuncture sustained needle prick injury while trying to recap an injection needle. Similarly, two of the laboratory HCWs had accidental blood splash during centrifugation for grouping and cross-matching of blood sample of a confirmed Lassa fever patient. They did not perfume hand hygiene immediately after the splash exposures nor reported the incidents to their supervisors as recommended in the IPC guidelines. None of the 19 HCWs recorded direct physical contact with a rodent in their households. One HCW travelled to a Lassa fever endemic area to care for a household member with febrile illness, three weeks prior to his onset of Lassa fever symptoms. The household member was later confirmed as a Lassa fever case but died subsequently after exposure with the HCW. None of the HCWs participated in either supervised or non-supervised burial within their communities.

Practice and compliance to standard/transmission-based precautions

Seventeen (89.5%) of the 19 HCWs investigated worked in shift duties in their respective treatment centers. Of this, five (29.4%) reported to have used full PPE (gloves, face mask, overall gown, apron & boot). They also reported performing hand hygiene (HH) with soap and water after such procedures. However, the two HCWs who had blood splash only used hand gloves during such procedures. They reported non-availability of full sets of PPE and absence of running water in the laboratory as hindering factors for their non-compliance to standard practice. While one HCW didn't always use full PPE while attending to patients in the Lassa fever treatment centers, one had records of lack of formal training on PPE use as a reason for non-compliance. Three HCWs worked in a private hospital and provided various nursing care without using any form of PPEs or performed HH after such procedures.

Infection prevention and control (IPC) training status

Out of the 19 HCWs reported, 14 (73.7%) of them never had any form of general IPC or Lassa fever specific PPE training in the last one year prior to their infection. Three of them had general IPC training in the past year of 2018, while only two had Lassa fever specific PPE training between 2017 and 2018.

Outcome of lassa fever HCWs infections

Two of the HCWs died while on admission, CFR of 10.5%. Both were female, a nurse and auxiliary nurse. The nurse worked in a public hospital, had been on self-medication for malaria and URTI prior to her presentation at the TC. She presented with a sore throat and dysphagia. The duration between onset of her symptoms to when she first sought medical attention was 10 days and died 10 days after admission. The auxiliary nurse presented with symptoms of fever, sore

throat, headache and epigastric pain and was also on self-medication for Malaria/URTI. The duration between onset of symptoms and presentation at TC was four days, while she died on the twelfth day of admission to the treatment centers. There were no observed major complications of Lassa fever such as coma, acute kidney failure (AKF), bleeding diastasis, hearing loss seizures among them during their hospitalization period and prior to their death. The other 17 HCWs survived the infection without any major complication. Seven of them completed their full complement of IV Ribavirin medication for 10 days while the remaining 10 had IV Ribavirin for average duration of six days and were later subsequently discharged on oral Ribavirin medication following a negative repeat PCR test.

Discussion

This paper describes the pattern of exposures, clinical features and outcome of LASV infections among HCWs in the 2019 outbreak. There are several factors and dimensions associated with the possible exposures for the 19 HCWs. Out of the 19 HCWs infections reported, 17 (89.5%) of them who had contact with and provided at least one form of care to Lassa fever patients, were likely to have contracted the disease through HTH transmission. The median duration of nine days from onset of symptoms to when the HCWs first sought medical attention, posed a serious challenge to control efforts and indicates a low index of suspicion for Lassa fever among these HCWs. The late commencement of IV Ribavirin further delayed their recovery as evidence has shown that Ribavirin is most effective in the management of LASV infections when commenced within the first six days of infection [15-17]. This finding is supported by the case report of the Lassa fever outbreak in Liberia, 2018 which highlighted the difficulty of timely detection and diagnosis of Lassa fever at primary health centers due to non-specific clinical features of the disease. Lassa fever presents with fever, like malaria which is endemic in many countries that also experience Lassa fever outbreaks. This has led to late detection and initiation of treatment [18]. Similarly, this finding was reported in a cluster of nosocomial Lassa infections in a tertiary health facility in Nigeria in 2018 where Lassa fever was not considered as a differential diagnosis, in either the index case, or among other HCWs who later presented to the tertiary facility with symptoms that could indicate potential LASV infection [19]. A recent 2019 report by World Health Organization (WHO) of a Dutch doctor who performed a surgical operation on a patient, and became symptomatic and was evacuated nine days later, after failing to respond to malaria/typhoid fever drugs, without any suspicion for Lassa fever, further supports our finding which shows that most of the HCWs had a low index of suspicion for Lassa fever and were instead, treated for malaria at the beginning of onset of their symptoms. Edo and Ondo States had the highest number (five each) of HCWs affected. This may be related to the fact that the two States have the highest burden of Lassa fever in Nigeria. We found that doctors were more affected (nine) than other categories of HCWs, like previous findings by Dan-wafor, et al. [20], where 50% of the affected HCWs were doctors. This could be suggestive of poor IPC compliance among doctors. The importance of this is that in a Lassa fever endemic area, HCWs should have a high index of suspicion for inclusion of Lassa fever among common differential diagnosis of any febrile illness that presents at treatment centers [19]. It also indicates that even at specialty centres, physicians could miss the diagnosis of Lassa fever as one of the HCWs who presented with fever, sore throat and back pain was seen by an ear, nose and throat (ENT) and orthopedic surgeons for more than a week before a suspicion for Lassa fever was made.

Another important factor associated with the likelihood of LASV infection among HCWS is poor knowledge of IPC and non-compliance to practice within treatment centers. The fact that only three out of 19 HCWs had general IPC training and only two had Lassa fever specific PPE training in the past poses a high risk to Lassa fever control measures. This means HCWs manage patients or blood samples, without adequate knowledge of IPC measures. Furthermore, the continuity in practice by two HCWs who recapped needles and sustained needlestick injuries justifies the need for constant adherence to standard precautionary measures like injection safety procedures. This observation has been consistent with several studies that found poor knowledge and practice of IPC measures, irrespective of the level of health facility in Nigeria [21,22]. Although similar studies have not reported exposures in the laboratory, our findings revealed that the two HCWs who had blood splash could have avoided that if facial protection was worn. This finding also always signifies a need for laboratories to have biosafety protocols in place and comply with their use. Given that two HCWs never provided care for any Lassa fever patient in the hospital and they could also not identify possible community exposures, genetic studies would be needed to further characterise patterns of transmission among Lassa fever infected HCWs.

Nosocomial spread of Lassa fever and infectious diseases can jeopardise the public trust for hospital visitations which has serious economic consequences on such heath facilities. This also has consequences on health seeking behavior, with a potential of hampering the overall patient safety in a hospital environment [23,24]. At the beginning of the 2019 outbreak and following preliminary findings from the HCWs infection, NCDC rapidly deployed its RRT members to support various interventions across the treatment centers to halt further HTH transmission. The NCDC RRT conducted various forms of on-site capacity development programs includ-

ing hands on training on standard/transmission-based precautions, improved patient management and risk communication for reducing stigma associated with Lassa fever infections. Lassa fever treatment centers were supported with PPE, outbreak response commodities and other consumables to strengthen IPC measures and case management in the treatment centers. To further enhance capacity of HCWs across the country, NCDC case management experts engaged various professional groups and provided them with guidelines for detecting and managing Lassa fever cases in the context of infection prevention and control.

Limitations

There were few limitations encountered in this study. RRT members could not extract some possible exposure histories from secondary data. Secondly, some information regarding the HCWs were not documented adequately from the case notes. Thirdly, we were unable to carry out genetic studies which could have linked HCWs to possible sources of LASV infections.

Conclusion

The exposure incidents and outcomes of the LASV infections described among the 19 HCWs supports the importance of adherence to IPC measures among frontline HCWs in health facilities. There is a growing need to plan targeted proactive interventions aimed at reducing the chances and likelihood of LASV infections among HCWs. These interventions should include pre-employment IPC training, in-service technical IPC orientation trainings for HCWs who will be working in the various Lassa treatment centers, intensive clinical fellowship for case management physicians, continuous sensitisation of professional bodies to increase index of suspicion and perception towards avoidance of potential predisposing factors to Lassa fever in the country, among other measures. The lessons from these exposure incidents should be applied in engaging HCWs for attitudinal change to improve their adherence to IPC measures, while providing healthcare services, especially in Lassa fever treatment centres.

Ethical Approval and Consent for Participation

This study was part of routine public health outbreak response, not research. Ethical approval was not required. However, a waiver for publication was sought from National Health Research Ethics Committee (NHREC).

Availability of Data

The datasets used and/or analysed during this study are available from the corresponding author on request.

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