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A cluster of nosocomial Lassa fever cases in a tertiary health facility in Nigeria: Description and lessons learned, 2018

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ABSTRACT

Background: Lassa fever is an acute viral haemorrhagic disease endemic in Nigeria. The 2018 Lassa fever outbreak in Nigeria was unprecedented, with 8% of all cases occurring among healthcare workers (HCWs). A disproportionately high number of these infections occurred in HCWs working in a tertiary health facility in Nigeria. This paper describes the cluster of Lassa fever infections among HCWs in a treatment centre and the lessons learnt.

Methods: We analysed clinical, epidemiological and laboratory data from surveillance and laboratory records kept during the 2018 outbreak. Interviews were conducted with surviving HCWs using a questionnaire developed specifically for the investigation of Lassa fever infections in HCWs. Descriptive analysis of the data was performed in Microsoft excel.

Results: The index case was a 15-year-old male who presented at the health facility with fever and uncontrolled nasopharyngeal bleeding, following a recent uvulectomy by a traditional healer. Overall, 16 HCWs were affected (15 confirmed and 1 probable) with five deaths (CFR-31.6%). Of the 15 confirmed cases, five (33.3%) were asymptomatic. Nine HCWs were direct contacts of the index case; the remaining six HCWs had no direct contact with the index case. HCW interviews identified a low index of suspicion for Lassa fever leading to inadequate infection prevention and control (IPC) practices as possible contributing factors to nosocomial transmission.

Conclusion: Maintaining a high index of suspicion for Lassa fever in all patients, especially in endemic areas, is essential in adhering to adequate IPC practices in health facilities in order to prevent nosocomial transmission of Lassa fever among HCWs. There is a need to continually train and sensitise HCWs on strict adherence to IPC measures while providing care, irrespective of a patient's provisional diagnosis.

Abbreviations: A&E, accident & emergencies; CFR, case fatality rate; ENT, ear, nose and throat; EOC, Emergency Operations Centre; IEC, information, education and communication; HCW, health care worker; IPC, infection prevention and control; LTFU, lost to follow up; NCDC, Nigeria Centre for Disease Control; PEP, post-exposure prophylaxis; PPE, personal protective equipment; PQDA, participatory quality development approach; RT-PCR, RT reverse-transcriptase polymerase chain reaction; VHF, viral haemorrhagic fever; VHF-CIF, viral haemorrhagic fever case investigation form.

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Background

Lassa fever is a viral haemorrhagic disease caused by a single-stranded RNA virus belonging to the family *Arenaviridae*. Lassa fever is a zoonotic disease, whose main reservoir is *Mastomys natelensis* which are capable of excreting the virus through urine, saliva, excreta, and other body fluids (Fisher-Hoch et al., 1995; Gunther and Lenz, 2004; WHO, 2018). Lassa fever is endemic in West African countries — mainly Nigeria, Sierra Leone, Ghana and Liberia. An estimated 100,000 to 300,000 cases are reported annually in this region of Africa, with 5,000 resulting in death, with sporadic cases reported in other African countries (McCormick et al., 1987). The incubation period of Lassa fever ranges from 6–21 days, signs and symptoms are non-specific and difficult to distinguish from other common febrile diseases such as malaria, especially early in the course of the disease (Dahmane et al., 2014; WHO, 2018). In its severe form, Lassa fever can manifest as a viral haemorrhagic fever and shock and multiorgan dysfunction can result, leading to death. However, approximately 80% of Lassa fever cases are thought to be mild or asymptomatic and often are unrecognized clinically (Bond et al., 2013; Enria et al., 2011; Inegbenebor et al., 2010; WHO, 2018). Approximately 1% of Lassa fever cases result in mortality (Ogbu et al., 2007; WHO, 2018). However, up to 20% of all patients with Lassa fever hospitalized for severe infection will die within 2 weeks of illness onset (Ogbu et al., 2007; WHO, 2018).

Transmission commonly occurs through direct contact with food or household items that have been contaminated with the urine or faeces of infected asymptomatic *Mastomys* rats. Rodent-to-human transmission of Lassa virus occurs when humans ingest, inhale, or have direct contact with rat urine or faeces, as when killing and processing an infected rat for consumption. However, person-to-person transmission can occur via direct contact with the blood or bodily fluids of infected patients and is a risk for health care workers (HCWs) involved in caring for Lassa fever cases. Although most Lassa fever cases occur as a result of zoonotic spill over into human populations, clusters of suspected nosocomial transmissions have been reported, particularly in health care settings (Gunther and Lenz, 2004). A high prevalence of antibody to Lassa virus in HCWs has been demonstrated in locations where there was a current or recent outbreak of the disease (Bajani et al., 1997). Nosocomial outbreaks have often been attributed to a lack of strict infection control practices and use of personal protective equipment (PPE) by HCWs, while providing health care (Fisher-Hoch et al., 1995; Hamblion et al., 2018). The first reported case of Lassa fever in Nigeria was a nosocomial infection in January, 1969, when a missionary nurse became ill at her station in Lassa town, North-Eastern, Nigeria (Carey et al., 1972; White, 1972).

In Nigeria, a number of Lassa fever case management centres, often called treatment centres, operate in association with specialist teaching hospitals in endemic states which typically report the highest number of Lassa fever cases each year.

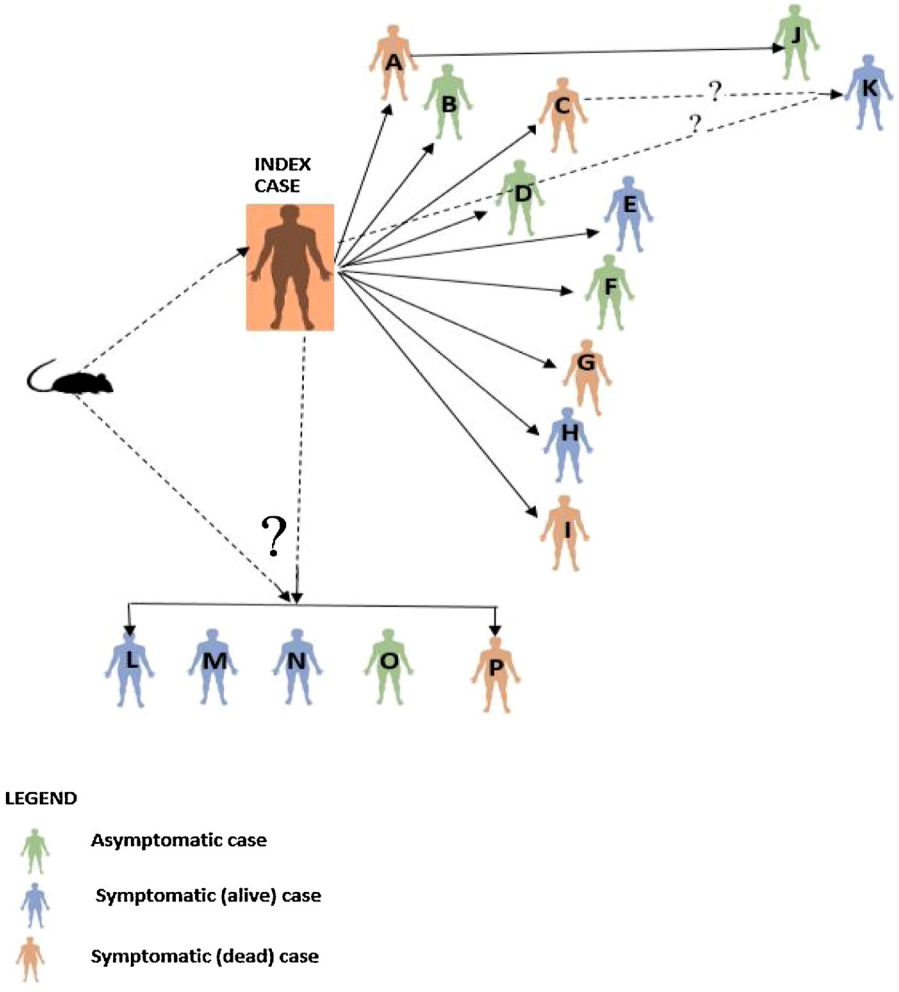

Figure 1. Lassa fever chain of transmission among HCWs in a tertiary health facility, Nigeria, 2018.

The scale of the 2017/2018 Lassa fever outbreak in Nigeria was unprecedented; heralded by an initial report of a cluster of cases and deaths among HCWs in a tertiary health facility by week 2 of 2018. By week 19 of 2018 when the emergency phase of the outbreak was declared over, a total of 1914 suspected cases had been reported from 21 states across Nigeria. Of these, 481 (25.1%) were laboratory confirmed with a case fatality rate (CFR) of 25.5% among the confirmed cases (NCDC, 2018). HCWs constituted 39 (8.1%) of all confirmed Lassa fever cases in the 2018 Lassa fever outbreak. Of all the Lassa fever confirmed cases among HCWs, 16 (41.0%) were reported from one tertiary health facility even though the state reported 65 (13%) of all Lassa fever confirmed cases nationally. This disproportionately high number of Lassa fever cases among HCWs at the health facility was investigated. This paper describes this cluster and provides lessons learned to prevent similar clusters occurring during future outbreaks.

Methods

The Nigeria Centre for Disease Control (NCDC) was notified of a cluster of cases and deaths among HCWs in a tertiary health facility. This cluster of cases was linked to a probable case who presented at the tertiary health facility December 2017. A rapid response team was immediately deployed to investigate the outbreak.

Case definition

For the purposes of this investigation we defined **HCWs** as all personnel working in health facilities regardless of whether they are in core clinical services, supportive functions or in training. Lassa fever cases were defined using the national Lassa fever preparedness guidelines (NCDC, 2017).

A **suspected Lassa fever case** was defined as any individual presenting with one or more of the following: malaise, fever, headache, sore throat, cough, nausea, vomiting, diarrhoea, myalgia, chest pain, hearing loss and either: (a) history of contact with excreta or urine of 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/haemorrhage from January 2018 in the State.

A **confirmed Lassa fever case** was any suspected case with laboratory confirmation (positive IgM antibody, PCR or virus isolation). Any suspected case who died or absconded without collection of specimens for laboratory testing was classified as a **probable Lassa fever case**.

Case finding

HCWs affected by Lassa fever were identified through interviews, retrospective record review and review of laboratory records. Patient case notes, and hospital admission and discharge registers were also reviewed by the rapid response team. Viral haemorrhagic fever case investigation forms (VHF-CIFs) were completed for all suspected HCW Lassa fever cases by disease surveillance officers and clinical management team. Detailed interviews were then conducted with surviving HCWs who had received a laboratory-confirmed diagnosis of Lassa fever using a questionnaire developed for the investigation of Lassa fever infections among HCWs. During interviews, HCWs were asked about their symptoms and hospitalisation, their history of contact with hospitalised Lassa fever cases, infection prevention and control (IPC) measures taken by the HCW and any potential community exposures (Figures 1 and 2).

Diagnosis

Blood samples were collected from some suspected cases meeting the case definition of Lassa fever and laboratory confirmation was performed using Lassa virus specific real time reverse-transcriptase polymerase chain reaction (RT-PCR) (Asogun et al., 2012) (Figure 3).

Data analysis

We performed a descriptive analysis of data, including demographics, clinical and risk factor information using Microsoft Excel (Table 1).

Results

Index case description and HCW exposure

The index case was a 15-year-old boy who was admitted in the health facility on 28th December 2017. On presentation, the patient was unconscious, febrile and was bleeding profusely from the mouth and nose. He had reportedly undergone an uvulectomy by a community healer seven days prior to admission. Partial or complete removal of the uvula is a traditional practice common in some groups in areas of sub-Saharan Africa, including Nigeria, where it is believed to aid in the management of throat related symptoms including throat pain and dysphagia (Adoga and Nimkur, 2011). The index case was then taken to a herbalist

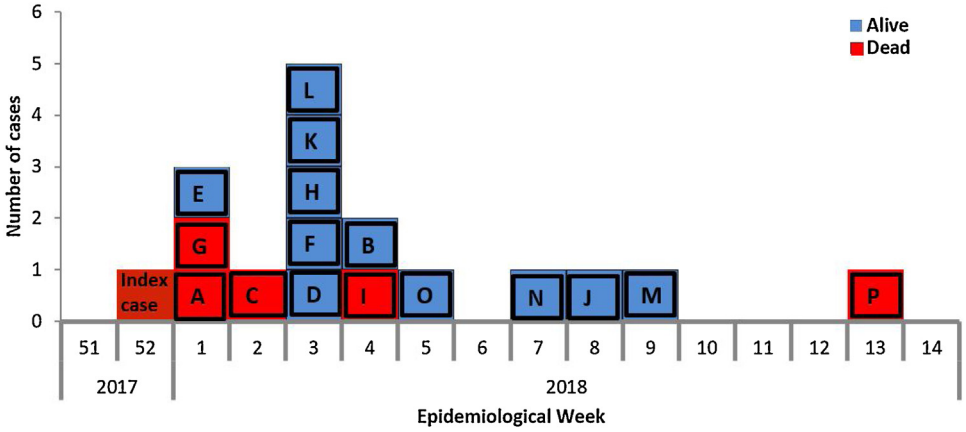

Figure 2. Epidemic curve of Lassa fever cases among HCWs in a tertiary health facility, Nigeria, 2018.

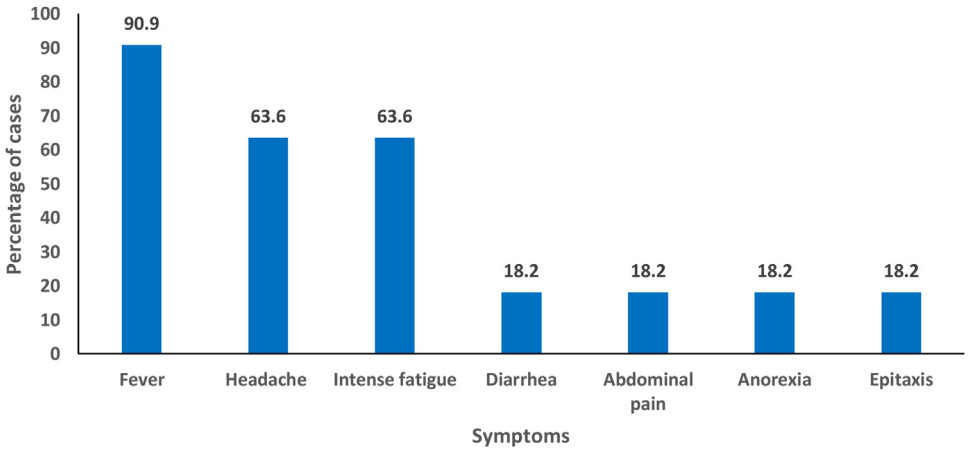

Figure 3. Distribution of symptoms among Lassa fever confirmed HCWs in a tertiary health facility, Nigeria (n = 11*).
*Five (5) HCWs were symptomatic.

Table 1
Characteristics of Lassa fever cases among HCWs in a tertiary health facility, Nigeria, 2018 (N = 16).

Characteristic	Number (Dead)	Percentage (%)
Sex		
Female	5 (1)	31.3
Male	11 (4)	68.8
Age (years)		
Median	37.5	
Range	20–51	
Category of HCW		
Doctor	8 (2)	50.0
Nurse	4 (1)	25.0
Nursing student	1 (1)	6.3
Medical student	1 (0)	6.3
Medical laboratory student	1 (0)	6.3
Orderly	1 (1)	6.3

where he spent five days before presenting to the health facility as his condition worsened. He was first reviewed in the Accident and Emergencies (A&E) ward by a doctor (HCW A) and a medical student (HCW B) whose role was to clerk the patient. Following this assessment, the patient was referred to the Ear, Nose and Throat (ENT) team on-call, who took over the management of the patient. Another doctor in the ENT department (HCW C), assisted by a nurse (HCW D) and a house officer (HCW E) took the case to theatre for further examination of his symptoms, with HCW C leading the surgical team. Two doctors (HCW F and H) with a nurse (HCW G) administered anaesthesia and assisted with the surgical procedure. An orderly (HCW I) cleaned the theatre following the surgical procedure performed on the index case.

At the time of the surgical procedure, Lassa fever was not considered as a possible differential diagnosis for the patient's symptoms; as a result, appropriate PPE was not used by the HCWs involved in the care of the index case. This was despite the patient having developed haemorrhagic symptoms. Medical and anaesthetic staff involved in the treatment of the index case reported performing a general examination, throat examination, cannulation, patient transportation and handling of the dead body (as the patient died on the same day of procedure) without appropriate PPE. Three HCWs (E, F and H) specifically reported sustaining blood splashes to unbroken skin and clothes while providing care to the index case. The index case died in the tertiary health facility on the same day; he did not receive a safe burial. None of the HCWs who had been exposed to the index case were offered post-exposure prophylaxis (PEP) with ribavirin for Lassa fever, as there was no suspicion of Lassa fever at the time.

HCW illness among contacts of index case

Six days after his review of the index case, HCW A developed symptoms including fever, diarrhoea, fatigue and abdominal pain. On 4th January 2018, he was admitted in a private health facility (Health Facility A) in a neighbouring town, and treated for suspected malaria. On 11th January 2018, he was admitted to the health facility after going into acute renal failure. Severe Lassa fever was suspected and he was then referred on to a specialist treatment centre with more established expertise in the management of complicated Lassa fever cases. He was accompanied by a nurse (HCW J) during his transfer. He died while an inpatient at the Lassa fever specialist treatment centre on 14th January 2018 and received a safe burial.

HCW C began developing symptoms on 9th January 2018. He was admitted on 12th January 2018 and treated for both diabetes and Lassa fever. He died on 14th January 2018. HCW G and HCW H who had also assisted in theatre on the 28th of December, both developed symptoms on 3rd January 2018 and 5th January 2018 respectively. They were initially admitted to the treatment Centre and then transferred to the Lassa fever specialist treatment centre. HCW G died within 24 h of referral, while HCW H made a full recovery.

On 21st January 2018, a community death notification of HCW I was received. Laboratory confirmation was never performed, but he was considered a probable case of Lassa fever given his exposure to the bodily fluids of the index case.

Additional HCW Lassa fever cases not directly related to index case

A further six confirmed Lassa fever cases were reported among HCWs working in the tertiary health facility, not thought to be associated with direct contact with the index case described above. The onset date of symptoms for these six individuals range from 15th January 2018 to 25th February 2018. These cases included: (a) a member of staff working in the laboratory (HCW O); (b) a senior registrar (HCW K) in general medicine, who attended to a patient the next day in the same theatre as the index case and who also had contact with HCW C when he became symptomatic; (c) a house officer in the paediatric unit (HCW L); (d) a clinician (HCW M) who did not report treating any suspected Lassa fever cases; (e) a nurse working in the isolation unit (HCW N), who was directly involved in the care of Lassa fever patients; and (f) a nursing student (HCW

P) whose uncle worked at the A&E unit and who eventually died at the isolation centre with an unclear source of infection.

Laboratory testing of HCWs who were contacts

Following the wave of Lassa fever infections and related deaths in HCWs at the health facility, 17 of the 118 HCWs who were line listed as contacts of the index case and subsequent confirmed cases in the state but were asymptomatic had their blood tested for Lassa fever. These 17 asymptomatic HCWs were concerned about being infected with the virus after having been exposed to HCW A and seeing other HCWs who had been exposed to the same patient becoming infected, some of whom had died. Of the 17 asymptomatic HCWs (contacts) who sought testing for Lassa fever, 5 (29.4%) — HCWs B, D, F, J and O — tested positive for Lassa fever (by PCR). Despite the absence of symptoms, HCWs B, F and J received a complete dose of ribavirin for PEP. HCW O received an initial intramuscular dose at the Lassa fever specialist treatment Centre and later continued on tablets by self-medication. HCW D was unaware of the positive result and was initially lost to follow up (LTFU); he was however found 2 weeks later but never received treatment.

None of the affected HCWs reported anyone in their household experiencing a febrile illness, being diagnosed with Lassa fever or dying within the 21 days prior to their own symptom onset. Only HCW N who worked on the Lassa fever treatment centre reported noticing rats in their residence within the 21 days prior to symptom onset.

Overall 16 HCW Lassa fever cases were reported from the health facility and its associated treatment centre (15 confirmed, 1 probable) with 5 deaths (CFR 31.6%). Of the 15 confirmed cases, five were asymptomatic (33.3%).

Lassa fever cluster chain of transmission

The diagram illustrates the likely rodent to human source of Lassa fever infection of the index case and the other HCWs who had no direct contact with the index case and transmission links from the index case to the HCWs who had both direct and indirect contact with the index case.

Epicurve of symptom onset date

Based on symptom onset date, the cluster peaked at epidemiological week 3 with the largest number of deaths occurring among cases in weeks 1 and 2, subsequently four cases with date of onset in weeks 7, 8, 9 and 13 were recorded. Most of the cases were reported earlier in the outbreak demonstrating the HCW vulnerabilities when surveillance and IPC measures were less than optimal.

Demographics of affected HCWs

The median age of the HCWs was 37.5 years ranging from 20 to 51 years. Majority of the HCWs were males 11(68.8%). The most affected category of HCWs was doctors 8(50%) followed by nurses 4 (25%).

Symptoms reported by affected HCWs

The most frequently reported symptoms by the HCWs were fever (90.9%), headache and fatigue (63.6%). The least symptoms were diarrhoea, anorexia, abdominal pain and epistaxis (18.2%).

Discussion

This paper describes a cluster of Lassa fever infections among 16 HCWs working in tertiary facility and an associated Lassa fever treatment centre in Nigeria. Ten of the 16 HCW infections are likely to have directly resulted from contact with a single case. Of the 16 HCWs who were infected in this cluster, five died — a CFR of 31.6%.

There are several factors that may have contributed to the spread of Lassa fever among HCWs. The first of these is that Lassa fever does not appear to have been 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 Lassa fever. While the 2018 Lassa fever outbreak was by far the largest outbreak ever recorded in Nigeria, Lassa fever is endemic across the country and HCW infections had previously been reported in a tertiary facility (Ajayi et al., 2013). Although the index case presented with apparent complications of an uvulectomy, the general health condition of the patient, the fever and the uncontrolled nature of his nasopharyngeal bleeding is more suggestive of a haemorrhagic fever. The lack of diagnosis or suspicion that the index case may have had Lassa fever was a critical factor in the nosocomial transmission of the infection to HCWs working in departments across the tertiary facility primarily because of insufficient use of PPEs, as well as other IPC precautions or inappropriate isolation of the patient. If Lassa fever was suspected, the HCWs involved in the index patient's care may have considered the need for adequate PPE and other IPC precautions such as appropriately isolating the patient. Consequently, the vast majority of subsequent HCW infections might have been avoided. Indeed, more cases of Lassa fever among HCW were reported earlier in the outbreak demonstrating the HCW vulnerabilities when surveillance and IPC capabilities and skills were less than optimal.

Some HCWs who were involved in assessing the index case at presentation to the A&E ward and who were involved in pre-operative preparations and assistance in the operative procedure, reported not being trained in the use of PPE and therefore did not use appropriate PPE. Nosocomial transmission of Lassa fever among this group of HCWs probably resulted from inadequate IPC measures, particularly inappropriate use of PPE, in both A&E and during surgery. The response to nosocomial infection requires timely investigation together with astute epidemiological and laboratory capabilities.

Infection of a HCW household member raises the question regarding risks of HCWs to their household members and by extension, members of the community and the need to protect them. Notably, only two of the 16 HCWs who became infected worked in the Lassa fever treatment unit. This suggests that there is a need to improve on existing knowledge of Lassa fever, transmission, signs and symptoms and importance of applying appropriate IPC measures among other hospital departments, outside of the Lassa fever treatment unit. This is particularly important given the fact that there are multiple patient entry points in the hospital, i.e. paediatric A&E, adult A&E, outpatient departments and the antenatal clinic. Patients will not conventionally self-report to the Lassa fever treatment unit. It is therefore logical that appropriate IPC training should be provided to hospital staff working at these patient entry points, together with the staff of other departments where patients will most likely be referred so that similar incidents can be avoided in the future. Special attention should also be paid to implementation of IPC measures and provision of the appropriate IPC equipment across the facility, which are factors that will reduce the risk of nosocomial infections.

The commonest symptoms among the HCWs were fever, headache, fatigue, and abdominal pain; these symptoms are consistent with findings from other studies (Bausch et al., 2001; Ehichioya et al., 2012; Macher and Wolfe, 2006; Okokhere et al., 2018). However, five of the 16 cases in this HCW cluster (31.3%) were asymptomatic, and would have been missed if the attending HCW did not have an increased risk perception at time of presentation. Given that up to 80% of Lassa fever infections are thought to be mild or asymptomatic (Bond et al., 2013; Enria et al.,

2011; McCormick et al., 1987; WHO, 2018), it is likely that other HCWs working at the tertiary health facility may also have been infected with the Lassa virus but did not exhibit any symptoms of the disease. It is unclear what the role of these HCWs may have been in the chain of transmission, although four of the five asymptomatic cases had direct contact with the index case. Further research is needed to characterise asymptomatic cases and identify their role in the transmission chain of Lassa fever infection.

Following the infections and deaths of many colleagues, 17 HCWs proactively sought Lassa fever testing outside of the standard Lassa fever testing protocol. This suggests that additional support needs to be provided for HCWs who have been directly involved in the care of Lassa fever patients, together with other staff working in healthcare facilities who may witness colleagues becoming infected with Lassa fever, and potentially dying from the disease. This support might include counselling and the provision of information that is targeted towards the key concerns that HCWs are likely to have.

The economic implications of VHF outbreaks in hospital are significant yet preventable (Aitken and Jeffries, 2001). Nosocomial transmission of Lassa fever has the potential to reduce public trust in the ability of a health facility to provide appropriate care, and may result in public avoidance of the healthcare system given the stigma associated with Lassa fever.

Nosocomial transmission of viral haemorrhagic fever (VHF) has often been attributed to clear deficiencies in IPC (Aitken and Jeffries, 2001). Following the outbreak, intensive efforts were made to strengthen IPC in the hospital. Complementary capacities in epidemiology and laboratory diagnosis were also strengthened given the challenges encountered in investigating this outbreak.

This incident led to an increased focus on improving IPC practices across the country and in turn necessitated the review of the existing national VHF IPC guideline. A new IPC training module was developed for frontline health care workers, using the participatory quality development approach (PQDA) to train the HCWs as 'IPC change agents'.

In response to this cluster of HCW infections, a remedial multi-disciplinary rapid response team deployed to the State-established an Emergency Operations Centre (EOC). Specific case management, IPC and safe burial teams were designated to ensure effective coordination of IPC strategies. The IPC committee of the tertiary facility was reactivated and the entire workforce received IPC training, with an emphasis on transmission-based precautions for staff working in the Lassa fever treatment centre. In addition, the isolation centre was renovated and re-modelled to comply with IPC standards: (a) hand hygiene infrastructure was installed at strategic positions across the facility, information, education and communication (IEC) materials were developed and displayed across the facility, the facility's waste management system was reviewed; (b) the laboratory received a biosafety cabinet to improve safety operations in the laboratory. PPE and other IPC consumables were also supplied to the Lassa fever treatment centre, together with the dissemination of guidelines on case management, IPC and response preparedness. Finally, in order to strengthen the capacity of the States to respond to Lassa fever outbreak, a national intensive clinical workshop on the diagnosis and management of Lassa fever was conducted for specific frontline HCW and surveillance officers, attended by key staff from hospitals, treatment centre and State ministry of health public health departments.

Limitations

This study was not without limitations. Firstly, the index case was defined as a probable case. This is because Lassa fever was not suspected when he initially presented and therefore a sample was not collected for laboratory confirmation before he died. Furthermore, we were unable to carry out genomic sequencing to determine the source of infection of the HCWs who were not directly linked to the index case. More efforts are needed in this regard for future outbreak investigation. Finally, there may have been recall bias among HCWs regarding their exposure, given the time lag between their onset of symptoms and varying exposures with the index case.

Conclusion

This cluster of Lassa fever infections among HCWs in a tertiary health facility in Nigeria, demonstrates the importance of Lassa fever awareness among HCWs, and the potential risks to staff when they have a low index of suspicion for Lassa fever. These include, poor IPC practices which was a critical factor in the transmission of Lassa fever among HCWs in this cluster. Lessons learned from these incidents should be disseminated widely to other health facilities to forestall future nosocomial transmissions by strict daily adherence to IPC measures while providing care, irrespective of a patient's provisional diagnosis.

Ethics approval and consent to participate

This study was part of public health response of outbreak, not research. Ethical approval was not required.

Consent for publication

Not applicable

Availability of data and material

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

Competing interests

None

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Authors' contributions

CDN, OI, ES, CI, and EI conceptualised the study, coordinated field epidemiological investigation, drafted and critically reviewed the manuscript for important intellectual content.

WE, WU, MS, and SM drafted and critically reviewed the manuscript.

AA, GI, and IU drafted the manuscript and did the statistical analysis.

CU, WN, EOm, UA, NI, JA, DN, TG, RS, and EA conducted field epidemiological investigation data collection, and reviewed the manuscript.

RO, EOg, PN, JO, OO and CP coordinated field epidemiological investigation and critically reviewed the manuscript.

All authors have seen and approved the final version of the manuscript for publication.

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