LASSA FEVER: A CLINICAL AND EPIDEMIOLOGICAL REVIEW

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ABSTRACT
BACKGROUND
This review summarises the history, aetiology, clinical presentation, management and prevention of Lassa fever, with emphasis on the epidemiological findings from Nigeria.

METHOD
Relevant search of articles on “Lassa fever” published between 1969 and August 2012 was undertaken using PubMed, AJOL, and Google search. Similar articles from relevant textbooks and from websites of World Health Organization, Centre for Disease Prevention and Control, USA and Federal Ministry of Health, Nigeria were also retrieved and reviewed. Emphasis was placed on papers reporting findings from Nigeria.

RESULTS
Lassa fever is a viral haemorrhagic fever, caused by the Lassa virus and first reported in Lassa town, Borno State, Nigeria in 1969. The virus is transmitted by multi-mammate rats, and responsible for deadly epidemics of haemorrhagic fevers in the West Africa sub-region. Not less than 28 states in Nigeria and the Federal Capital Territory have witnessed outbreaks of Lassa fever in last five decades. Outbreaks in Nigeria are common in rural communities and in hospital settings, fuelled by socio-cultural practices, poor environmental and personal hygiene and poor practice of infection prevention and control. The clinical presentation is protean and diagnosis is often delayed. Ribavirin remains the only effective life-saving treatment only when given six days of onset of symptoms.

CONCLUSION
Lassa fever remains an important cause of morbidity and mortality in West Africa, Nigeria inclusive. Stakeholders in affected countries ought to strengthen surveillance and response to Lassa fever outbreaks, as well as strictly implement established preventive strategies.

Key words: Lassa fever; Multi-mammate rat; haemorrhagic fever; Epidemics; Nigeria

INTRODUCTION
Lassa fever is a rodent-transmitted viral haemorrhagic disease of global health concern. The disease is endemic in West African and responsible for recurrent epidemics of acute haemorrhagic fever in parts of West Africa as well as sporadic disease in Europe, Asia and America. The Lassa virus is a likely agent of bioterrorism, with capacity for person to person transmission and potential to cause hospital outbreaks with attendant morbidity and mortality among health workers.

This review summarises the history, aetiology, clinical presentation, management and prevention of Lassa fever, with emphasis on the epidemiological findings from Nigeria.

HISTORICAL BACKGROUND
The earliest cases of Lassa fever were thought to have occurred between 1920 and 1950, in Nigeria, Sierra Leone and Central African Republic and perhaps in other West African countries. However, the disease became recognised and named in 1960 after two missionary nurses died and a third suffered a grave apparently communicable febrile systemic illness while working in Nigeria. The index patient was working in a mission hospital in Lassa town, Borno State, North-Eastern Nigeria when she fell critically ill and was transferred to Evangel Hospital, Jos Plateau State (now Bingham University Teaching Hospital, Jos) where she subsequently died.

The second nurse, who was a staff of Evangel Hospital, cared for the index patient on presentation and she later developed comparable symptoms like the index case culminating in her death days later. The third nurse was also a staff of Evangel Hospital who cared for both patients. She also fell progressively ill and had to be transferred to the United States of America for further management and definitive diagnosis. Fortunately she survived and recovered almost completely except for scalp hair loss. Serum samples and body fluids retrieved from all these patients were later shown to be positive of a novel virus which was named ‘Lassa virus’ and the disease named ‘Lassa fever’ in recognition of Lassa town where the index case of
the disease was first documented.

**CAUSATIVE AGENT**
The Lassa virus is a single stranded RNA virus belonging to the Arenaviridae family of viruses. The virus is often named haemorrhagic fever virus because of the tendency to cause bleeding from body orifices. It is round, oval, or pleomorphic, 110 to 130 nm in diameter, and enveloped. Its genome consists of two single-stranded RNA segment - the large L segment and the small S segment. The large segment encodes the viral polymerase and zinc binding protein and the small segment encodes the structural proteins - nucleoprotein and glycoprotein precursor.

The virus is inactivated by heating from 56–100°C, ultraviolet and gamma radiations and pH range between 5.5 and 8.5, as well as by chemical agents like 0.5% sodium hypochorite, 0.5% phenol, 10% formalin and detergents. –

Sequencing of the small segment of the RNA of Lassa virus has revealed the presence of four major lineages in West Africa: three in Nigeria (lineages I, II, and III) and one in the area comprising Ivory Coast, Sierra Leone, Liberia, and Guinea (lineage IV). Various viral strains have been associated with these major lineages with differences their genetic, serologic, and pathogenic characteristics.

**RESERVOIR**
The natural reservoir for Lassa virus is the multimammate rat named *mastomys natalensis*. The Mastomys are peri-domestic rats that live in and around human settlements, leaving the bush for homes during bush burning or in search of food. They have some unique features which include characteristics foul odour, long hairless tail, soft body fur, pointed rostrum and ventral surface lined by multiple mammary glands [Figure 1]. They have an average life span of 2 years and breed round the year with each pregnancy resulting in 16-20 litres. Once infected, the rats do not become ill but shed the virus in their body fluids for the rest of their lives.

In Nigeria, mastomys natalensis have been identified by various names in some local languages including Eeku Asin (Yoruba), Jagba (Hausa), Nkapia or Nkakwu- (Igbo), and Isun (Kolokuma-Ijaw).

*Mastomys natalensis* is ubiquitous in equatorial Africa, found in east, west, central, north and southern Africa. – The wide distribution of Mastomys in countries outside the Lassa fever endemic zones of West Africa may indicate the existence of unrecognized and undiagnosed cases of Lassa fever in these regions or presence of other biological explanatory factors such as differences in virus susceptibility between subpopulations of Mastomys, regional differences in host susceptibility to the Lassa virus and perhaps the presence of an additional as yet unidentified primary reservoir host.

Ecological factors such as height, variability and seasonal timing of rainfall are other possible explanatory variables for the discordance in the Lassa fever and Mastomys distribution in Africa. Since most outbreaks of Lassa fever have been observed to occur in regions with annual rainfall above 1500mm, it has been suggested that the Lassa virus may survive better in humid conditions during the rainy season.

Studies have shown that the rodent host is more often contaminated during frequent movements in the rainy season and that villages where Lassa virus—infested rodents have been trapped are located in the rain forest areas or in transition zone between forest and savannah within 1500mm of annual rainfall.

Although rodent infection may occur more frequently in the rainy season, viral aerosol stability is higher when the humidity is lower, as seen during the dry season. Increased aerosol transmission of the Lassa virus, among other factors, may account for the occurrence of recurrent outbreaks of Lassa fever during the dry season in some regions.

**EPIDEMIOLOGY**
Lassa fever accounts for an estimated 200,000 to 500,000 cases and 5000 deaths yearly in West Africa, particularly in Sierra Leone, Nigeria, Liberia and Republic of Guinea. Serological evidence of Lassa fever has also been found in Mali, Senegal and Central African Republic. Sporadic imported cases have been reported in the United States of America, Europe and Asia, while laboratory infection has occurred among health workers in the USA during handling of infected specimens.

There is no age, gender or racial predilection. Outbreaks in endemic regions are promoted by factors that lead to increased rodent-man contact such as civil unrest (which lead to mass movement of people and rapid development of human settlements), crowding, poor sanitation, deforestation, rodent hunting, bush burning, and agricultural developments such as rice cultivation that provide food supplies for rodents. Rural dwellers in West
Africa are at risk of Lassa fever because of proximity to animal reservoir, open construction of African villages, the practice of drying grains by road sides or outside homes and unprotected grain storage within homes. All these factors are known to facilitate increased rodent-man contact or contamination of food sources by infected rodent secretions.

Hospital workers may be at risk of Lassa fever if proper barrier nursing and infection control practices are not maintained. However, it has been speculated, although not proven, that hospital outbreaks may also be facilitated by airborne transmission without need for close contact with infected patient.

Epidemiology in Nigeria
Lassa fever has accounted for recurrent outbreaks of acute haemorrhagic fever in Nigeria since the discovery of the virus in Lassa town northeastern Nigeria in 1969. The prevalence of antibodies to the virus in Nigeria is 21% as compared to 8-22% in Sierra Leone and 4-55% in Guinea. In the last 50 years more than 28 states in Nigeria and the Federal Capital Territory have experienced one or more outbreaks of Lassa fever. Tables 1 outline outbreaks of Lassa fever in Nigeria that have been reported in the literature and by the Federal ministry of health, Nigeria from 1969 to 2006. Outbreaks were also reported in various states in Nigeria between 2008 and 2011. The last outbreak of Lassa fever in Nigeria began in December 2011 and as at 17th August 2012, a total of 934 suspected Lassa fever cases, 147 Laboratory confirmed and 93 deaths (CFR 9.97%) were reported from 41 LGAs in 23 States (Figure 2). In states that have yet reported a case or an outbreak of Lassa fever since 1969, it is possible that cases of Lassa fever were either unrecognised or not reported.

Since 1969, when deaths of health workers in Nigeria led to the discovery of the Lassa virus, almost all subsequent outbreaks of Lassa fever have been characterised by collateral infection and deaths of health workers, including doctors, nurses and other allied health workers.

During the 2012 outbreak of Lassa fever in Nigeria at least three doctors and four nurses were reported to be among the fatalities.

Edo state has so far recorded the highest incidence of outbreaks of Lassa fever in Nigeria. This may be partly due to improve surveillance compared to other states, as one of the major diagnostic centres for Lassa fever in Nigeria is situated in Edo state. In a study conducted at Iruua Specialist Teaching Hospital, in Edo state, Lassa fever accounted for 7% of the admissions and 13% of deaths in the adult medical wards of Iruua Specialist Teaching Hospital in 2007. These rates are lower than the findings in a similar study in Sierra Leone in 1987, in which Lassa fever was found to be responsible for 10–16% of admissions and 30% of adult deaths in the medicine department of a major referral centre.

Certain cultural and personal habits have been implicated as factors promoting high incidence of Lassa fever in Edo State. These factors included use of rat meat as a source of protein by people in some communities, contamination of exposed food by rat faeces and urine, and traditional autopsy, where the operator may be injured with scalpel and the injury contaminated with the blood of the deceased. Other risk factors identified included forceful ingestion of water used in bathing a dead husband by a widow suspected to be involved in his death and practices of drying Gari (cassava flour) in the open air, where Lassa fever infected rodents contaminate the Gari while using it as a food source.

Transmission
Lassa fever is transmitted mainly through contact with infected secretions of rats. Humans get infected when infected rat secretions (excreta or urine) make contact with non-intact skin (e.g. through cuts or sores) or mucous membranes, and by ingestion of food or liquid contaminated by infected secretions, as well as by inhalation of aerosolized viral particles.

Human to human transmission of Lassa fever is common in hospital settings and usually follows contact with infected blood, urine, and other body secretions of patients with Lassa fever or through contact with contaminated hospital equipments, including reused needles. There is also the risk of sexual transmission since the virus is excreted in semen for up to three months after recovery from an acute illness. Airborne human to human transmission of Lassa fever has been speculated but supportive evidence remains inconclusive. In the 1970 Lassa fever outbreak in Evangel Hospital, Jos, Plateau state, Nigeria, airborne spread of the virus was suspected, and this was believed to have been facilitated by closely juxtaposed beds and by prevailing breeze which probably carried the aerosolized virus across the bed of the index case to the rest of the open ward.

Transplacental transmission from infected mother to unborn child is less frequently reported but it is associated
with poor prognosis for mother and fetus. The virus is usually not transmitted by asymptomatic infected individuals and cannot be spread through casual contact, including skin-to-skin contact without exchange of body fluids.

Pathogenesis
The pathogenesis of Lassa fever is underlined by unchecked viremia, microcirculatory instability and impaired haemostasis mediated by immunological mechanisms. The virus enters the human body through the bloodstream, lymph vessels, respiratory tract, and/or digestive tract. It then multiplies in the local tissues or in the cells of the reticuloendothelial system. Secondary dissemination occurs through lymph and blood monocytes to a wide variety of organ parenchyma and their associated mesothelial cell linings, including the liver, spleen, endothelium, lymph nodes, kidney, adrenal gland, pancreas, placenta, uterus, breast, and gonads.

In the development of symptomatic infection, interactions between the virus and immune cells (macrophages and dendritic cells) lead to activation of a cascade of inflammatory mediators including cytokines, chemokines and other vasoactive mediators, which in turn lead to cellular and endothelial dysfunction, increased vascular permeability and capillary leak, insufficient effective circulating intravascular volume and multi-system organ failure.

Although mild thrombocytopenia is a common feature, bleeding appears to be related to platelet dysfunction mediated by Lassa virus-induced release of a soluble mediator impairing platelet aggregation.

CLINICAL PRESENTATION
The varied clinical presentations of Lassa fever have been described by various authors. Only about 20% of persons infected by the Lassa virus develop symptoms, with the remaining 80% demonstrating serological evidence of infection without symptoms. The underlying determinants of variability in clinical presentation is unknown, although infecting dose, route of infection, virulence of viral strain, host immune response and background genetic predisposition are suggested explanatory variables deserving future confirmatory studies.

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Lassa fever is characterised by an acute illness of one to four weeks duration following an average incubation period of 10 days (range, 3–21 days). The onset of illness is typically gradual, with non-specific signs and symptoms such as fever, headache, anorexia, malaise, and generalized weakness. At this early phase, Lassa fever may mimic many other febrile illnesses that are common in the tropics and diagnosis is possible only with high index of suspicion.

After early non-specific symptoms, the first week of illness is characterised by sore throat with or without pharyngitis, conjunctival injection (without itching, discharge or rhinitis) muscle pain, retrosternal pain, dry cough, nausea, vomiting, diarrhoea, and abdominal pain. A maculopapular or petechial rash is usually noted over the thorax, face and arms in fair-skinned patients, but has not been noted in black Africans. By the second week severe cases may progress to show features of vascular instability such as facial swelling, proteinuria, fluid in the lung cavity, bleeding from mouth, nose, vagina or gastrointestinal tract, and low blood pressure. However, overt bleeding from body orifices is seen in less than 20% of hospitalised patients. Shock, seizures, tremor, disorientation, and coma may be seen in the late stages. In a prospective case control study of 441 hospitalised Lassa fever patients in Sierra Leone, the best predictor of Lassa fever was found to be the combination of fever, pharyngitis, retrosternal pain, and proteinuria (combined predictive value of 81%).

Without treatment mortality occurs by the 10th to 12th day of illness with case fatalities of 1–2% in the general population and 15-20% in hospitalised patients, rising as high as 50% during epidemics. Fatal illness follows unchecked fulminant viremia due to impaired and dysregulated cellular immune response. The clinical predictors of poor prognosis include shock, bleeding, neurological manifestations, high viremia (or surrogate measurements of antigen or genome copies), and levels of aspartate aminotransferase (AST >150 IU/l).

Lassa fever in pregnancy is characterised by high fetomaternal and neonatal mortality. Maternal mortality is worse at the third trimester of pregnancy while fetal mortality is highest during the first trimester. Neonatal Lassa fever is uniformly fatal. Infants may present with features of 'swollen baby syndrome' consisting of anasarca, abdominal distension, and bleeding, and associated with a high mortality. It has been suggested that the poor prognostic outcome of Lassa fever in pregnancy might be
due to higher concentrations of the virus in pregnant than in non-pregnant women, presence of high concentrations of the virus in the placenta and the relative immunosuppressive state of pregnancy.

Clinical sequelae of Lassa fever may include deafness, transient hair loss, cerebellar ataxia and depression. Majority of these symptoms occur during convalescent and are mostly immune-mediated. Deafness is sensorineural, bilateral or unilateral, affecting less than 25% of cases, permanent in two third of cases and not related to the severity of the illness or the level of viremia. The pathogenesis of deafness is believed to follow an immunological reaction between the circulating Lassa virus antibodies and the basal cell membrane /outer hair cells of the cochlear.

Survivors of Lassa fever may likely develop life-long immunity, at least against severe disease. However, the protective effects of prior infection in the prevention of future symptomatic disease have not been extensively studied in humans.

**Diagnosis and laboratory features**

The World Health Organisation has developed a case definition for diagnosis of Lassa fever for public health surveillance (see table 2). A confirmed case of Lassa fever is defined as any case with compatible clinical presentation with positive laboratory diagnosis of Lassa fever.

Lassa fever is most often diagnosed by using enzyme-linked immunosorbent serologic assays (ELISA), which detect IgM and IgG antibodies as well as the Lassa antigen. ELISA assays are simpler, more specific and sensitive than immunofluoresence assays. The virus itself may be cultured in laboratory animals such as albino mice, guinea pigs, Vero cell or African green monkey in 7 to 10 days. Immunohistochemistry performed on tissue specimens can be used to make a post-mortem diagnosis. The virus can also be detected by reverse transcription-polymerase chain reaction (RT-PCR). Viral culture and RT-PCR are however not routinely done as they are research-based investigations reserved for biosafety level IV laboratories.

Common laboratory features of Lassa fever include mild thrombocytopaenia (not usually <100,000/l), mild leucopenia with lymphopenia, elevated blood urea nitrogen, elevated amylase and proteinuria. There is also elevated hepatic transaminase with level of AST significantly higher that alanine aminotransferase (ALT).

**Treatment**

Once Lassa fever is suspected, the patient should ideally be admitted into an isolation room or ward and barrier-nursed. Barrier nursing is a process of keeping a patient at bay and entails the use of infection control practices to control and prevent spread of pathogenic microorganisms to uninfected or susceptible individuals.

The isolation room should have an isolated toilet, adequate ventilation and screen window. In the absence of an isolation room/ward, patients can be kept in an area in a larger ward that is separate and far away from other patients in the ward.

After isolation, relevant health authorities should immediately be notified so that diagnosis can be confirmed as rapidly as possible and appropriate treatment commenced. Health workers and patient's relatives are expected to comply with strict infection control guidelines including use of personal protective equipments such as gowns, gloves, face masks, eye goggles and boots when in contact with patients or with their body fluids or their waste products. Standard guidelines for infection control of viral haemorrhagic fevers including Lassa fever in African setting has been published by the Centre for Disease Control (CDC), USA, in collaboration with the World Health Organisation (WHO). Table 3 summarises isolation precautions for suspected Lassa fever patients in hospital settings.

**Drug treatment**

The only specific effective treatment of Lassa fever is the antiviral drug named Ribavirin. The mechanisms of action of Ribavirin are not completely understood but it is known to have broad spectrum antiviral properties against both RNA and DNA viruses as well as immunomodulatory effects. Ribavirin is life-saving if given within six days of onset of symptoms, reducing mortality by as much as 90%. In view of delay in confirmatory laboratory diagnosis in most Lassa fever endemic countries, presumptive therapy can be initiated as soon as possible in patients with compatible clinical features pending diagnostic laboratory results. Ribavirin is given as a slow intravenous infusion (10-15minutes) starting with a loading dose of 32mg/kg, then 16mg/kg every 6 hrs for 4days, then 8m/kg every 8hrs for 6 days. Total duration of treatment is 10days.

Ribavirin is almost twice as effective when given
intravenously as when taken orally. Oral Ribavirin is the preferable option for Lassa fever post-exposure prophylaxis, especially among health workers and family members who might have been exposed to infected secretions during care of Lassa fever patients. There is however no consensus guidelines for use of oral ribavirin for post-exposure prophylaxis. Some authorities recommend PEP only in the event of a definitive high-risk exposure, defined as 1 of the following: (A) penetration of skin by a contaminated sharp instrument (e.g., needlestick injury), (B) contamination of mucous membranes or broken skin with blood or bodily secretions (e.g., blood splashing in the eyes or mouth), (C) participation in emergency procedures (e.g., resuscitation after cardiac arrest, intubation, or suctioning) without use of appropriate personal protective equipment, and (D) prolonged (i.e., for hours) and continuous contact in an enclosed space without use of appropriate personal protective equipment (e.g., a health care worker accompanying a patient during medical evacuation). The proposed oral regimen include a loading dose of 35-mg/kg loading dose (maximum dose, 2.5 g) followed by 15 mg/kg (maximum dose, 1 g) 3 times a day for 10 days. For a 70-kg adult, this translates to an approximately 2.4-g loading dose, followed by 1 g taken 3 times a day.

Ribavirin is potentially teratogenic and embryotoxic. However, due to high maternal and fetal mortality associated with Lassa fever during pregnancy, the benefits of Ribavirin treatment in pregnancy outweigh the risks. When Lassa fever occurs in pregnancy, the priority is to save the life of the mother as the fetus has only a one in ten chance of survival no matter the course of action taken.

The major adverse effects of intravenous Ribavirin are hemolytic anemia (usually mild to moderate and reversible) and rigors following rapid infusion of the drug. Some reported adverse reactions of oral ribavirin include anemia, nausea and vomiting, metallic taste, dry mouth, myalgia, fatigue, and diarrhoea, among others. Most of these symptoms are mild and all are reversible with cessation or dose reduction of the drug. Ribavirin is contraindicated in patients with chronic anaemia and haemoglobin levels below 8 g/dl, and in patients with severe renal impairment (creatinine clearance <30 ml/min).

**Supportive Non-drug treatment**

Non-specific supportive treatment may include symptomatic treatment of dehydration with fluid replacement and correction of anaemia by blood transfusions as necessary. Occasionally, some patients might benefit from antibiotics coverage for secondary bacterial infection.

**Prevention and control**

Lassa fever is a notifiable disease requiring active surveillance and rapid response to avert or abort epidemics. Primary prevention of Lassa involves avoidance of contact with infectious secretions of rodents as well as with body fluids or excreta of infected humans. The basic strategies for prevention of Lassa fever are summarised in table 4.

In Nigeria, the federal ministry of health and some state governments have established Lassa fever rapid response committees, responsible for co-ordinating a rapid response to Lassa fever outbreaks through active surveillance, case management, sensitization of hospital workers and the general public.

Unlike many other infectious diseases where preventive vaccines are available, there is yet no licensed vaccine for use in humans, although many candidate vaccines show promise in studies conducted in animals.
Figure 2: Map of Nigeria Showing Areas Affected By Lassa Fever As At August 17, 2012

Table 1: REPORTED OUTBREAKS OF LASSA FEVER IN NIGERIA 1969-2006.

<table>
<thead>
<tr>
<th>Year</th>
<th>States/cities affected</th>
<th>Cases</th>
<th>Deaths</th>
<th>Case Fatality Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1969</td>
<td>Borno (Lassa Town), and Plateau (Jos)</td>
<td>3</td>
<td>2</td>
<td>66.7</td>
</tr>
<tr>
<td>1970</td>
<td>Plateau (Jos and Vom)</td>
<td>28</td>
<td>10</td>
<td>58</td>
</tr>
<tr>
<td>1974</td>
<td>Anambra (Onitsha)</td>
<td>3</td>
<td>1</td>
<td>33.3</td>
</tr>
<tr>
<td>1975</td>
<td>Kaduna (Zookwa), and Plateau (Vom)</td>
<td>4</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>1980</td>
<td>Kaduna (Zaria)</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>1989</td>
<td>Imo</td>
<td>34</td>
<td>22</td>
<td>64.7</td>
</tr>
<tr>
<td>1993</td>
<td>Plateau</td>
<td>13</td>
<td>8</td>
<td>61.5</td>
</tr>
<tr>
<td>1994</td>
<td>Edo</td>
<td>20</td>
<td>11</td>
<td>55</td>
</tr>
<tr>
<td></td>
<td>Enugu</td>
<td>54</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Lagos</td>
<td>2</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>1995</td>
<td>Yobe</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Akwa Ibom</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Anambra</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1998</td>
<td>Anambra</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Rivers</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1999</td>
<td>Zamfara</td>
<td>46</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2000</td>
<td>Edo</td>
<td>60</td>
<td>26</td>
<td>43.3</td>
</tr>
<tr>
<td></td>
<td>Nasarawa</td>
<td>26</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2002</td>
<td>Edo</td>
<td>55</td>
<td>15</td>
<td>27.3</td>
</tr>
<tr>
<td></td>
<td>Lagos</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2003</td>
<td>Edo</td>
<td>31</td>
<td>18</td>
<td>58.1</td>
</tr>
</tbody>
</table>

Table 2: WHO CASE DEFINITION OF LASSA FEVER FOR EPIDEMIOLOGICAL SURVEILLANCE

A. Clinical description
- An illness of gradual onset with one or more of the following: malaise, fever, headache, sore throat, cough, nausea, vomiting, diarrhoea, myalgia, chest pain, hearing loss, and
- A history of contact with excreta of rodents or with a probable or confirmed case of Lassa fever.

NB: In Lassa fever endemic regions such as Nigeria, a suspected case is defined [23] as an illness with onset of fever and no response to treatment of usual causes of fever in the area and at least one of the following signs:
- Bloody diarrhoea
- Bleeding from gums, into skin (purpura) and into eyes
- Bloody urine

B. Laboratory criteria for diagnosis
- Isolation of virus (only in laboratory of biosafety level 4) from blood, urine or throat washings or
- Positive IgM serology or seroconversion (IgG antibody) in paired serum specimens or
- Demonstration of Lassa virus antigen in autopsy tissues by immunohistochemistry or in serum by ELISA
- Positive Polymerase Chain Reaction (PCR) from serum or autopsy tissues

C. Case classification
- Suspected: A case compatible with the clinical description.
- Probable: A suspected case that is epidemiologically linked to a confirmed case.
- Confirmed: A suspected case that is laboratory-confirmed.

Contact: A person having close personal contact with the patient (living with, caring for) or a person testing the laboratory specimens of a patient in the 3 weeks after the onset of the illness.

Table 3: WHO RECOMMENDED ISOLATION PRECAUTIONS FOR VIRAL HEMORRHAGIC FEVERS INCLUDING LASSA FEVER

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>1</td>
<td>Isolate the patient</td>
</tr>
<tr>
<td>2</td>
<td>Wear protective clothing in the isolation area, in the cleaning and laundry areas and in the laboratory. Wear a scrub suit, gown, apron, two pairs of gloves, mask, head cover, eyewear, and rubber boots.</td>
</tr>
</tbody>
</table>
3 Clean and disinfect spills, waste, and reusable equipment safely.

4 Clean and disinfect soiled linens and laundry safely.

5 Use safe disposal methods for non reusable supplies and infectious waste

6 Provide information about the risk of VHF transmission to health facility staff. Reinforcement use of VHF Isolation Precautions with all health facility staff.

7 Provide information to families and the community about prevention of VHF s and care of patients

NB: VHF- viral haemorrhagic fever

<table>
<thead>
<tr>
<th>Table 4: Strategies For Prevention Of Lassa Fever</th>
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<tbody>
<tr>
<td><strong>A. General Measures</strong></td>
</tr>
<tr>
<td>✓ Institution of policies, task force, committees for surveillance, prevention and control of Lassa fever at National and state level,</td>
</tr>
<tr>
<td>✓ Health education/sensitization of the public and health workers about the disease, transmission, manifestations and prevention,</td>
</tr>
<tr>
<td><strong>B. Rodent control</strong></td>
</tr>
<tr>
<td>✓ Avoid bush burning</td>
</tr>
<tr>
<td>✓ Setting traps in and around homes to reduce rat population</td>
</tr>
<tr>
<td>✓ Block all rat hideouts</td>
</tr>
<tr>
<td>✓ Avoid contact with rats e.g. 'rat hunting for consumption'</td>
</tr>
<tr>
<td>✓ Keep cats</td>
</tr>
<tr>
<td><strong>C. Individual and community preventive strategies</strong></td>
</tr>
<tr>
<td>✓ Keep good and healthy personal hygiene</td>
</tr>
<tr>
<td>✓ Clean your home and environment</td>
</tr>
<tr>
<td>✓ Empty waste far away from homes</td>
</tr>
<tr>
<td>✓ Do not spread food where rats can have access to it.</td>
</tr>
<tr>
<td>✓ Store foodstuff and water in rat proof containers</td>
</tr>
<tr>
<td>✓ Wash all foods, cook all foods properly</td>
</tr>
<tr>
<td><strong>D. Hospital based prevention</strong></td>
</tr>
<tr>
<td>✓ Adherence to infection control measures</td>
</tr>
<tr>
<td>✓ Isolation of infected patients</td>
</tr>
<tr>
<td>✓ Barrier nursing of infected patients</td>
</tr>
<tr>
<td>✓ Wearing protective clothing when caring for patients or working with secretions of infected patients e.g. masks, gloves, gowns</td>
</tr>
<tr>
<td>✓ Routine equipment sterilization</td>
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