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## ACCESSIBILITY TO LABORATORY DIAGNOSIS OF LASSA FEVER IN NIGERIA: A POSSIBLE THREAT TO THE CONTROL OF INFECTIOUS DISEASES

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### ABSTRACT

Lassa fever caused by lassa virus is an haemorrhagic infectious disease with limited access to diagnostic facilities in Nigeria. Lassa virus infections can only be diagnosed definitively in the laboratory using the following tests: reverse transcriptase polymerase chain reaction (RT-PCR) assay-gold standard, antibody enzyme-linked immunosorbent assay (ELISA), antigen detection tests and virus isolation by cell culture. Cases of this infectious disease have been reported in 24 of the 36 States in Nigeria. Currently, two national laboratories are supporting the laboratory confirmation of Lassa fever cases by polymerase chain reaction (PCR) tests. All the samples were also tested for Ebola, Dengue, Yellow fever and so far have tested negative. The two laboratories that are currently operational are: Virology laboratory, Lagos University Teaching Hospital, Lagos -Nigeria and Lassa fever research and control centre, Irrua specialist hospital/Lahor Research Laboratory, Edo State-Nigeria. Tertiary Institution Students and National Youth Corps are also affected. Lassa fever affects all sex, ages and socio-economic classes. Establishment of Laboratories for screening and Diagnosis of Lassa and other haemorrhagic diseases at tertiary academic institutions, primary, secondary and tertiary health care centers in Nigeria will reduce scourge of Lassa fever and other haemorrhagic diseases.

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### INTRODUCTION

The Lassa virus was first described in 1969 in the town of Lassa, in Borno State, Nigeria. Lassa fever is a zoonotic disease, meaning that humans become infected from contact with infected animals. The animal reservoir, or host, of Lassa virus is a rodent of the genus *Mastomys*, commonly known as the “multimammate rat.” *Mastomys* rats infected with Lassa virus do not become ill like commensals, but they can shed the virus in their urine and faeces [1-5].

Lassa fever caused by Lassa virus is an acute viral hemorrhagic fever. The virus is a member of the arenavirus family. Lassa virus is transmitted to humans from contacts with food or household items contaminated with rodent excreta. Furthermore according to WHO (2016) “Humans usually become infected with Lassa virus from exposure to urine or faeces of infected *Mastomys* rats. Lassa virus may also be spread between humans through direct contact with the blood, urine, faeces, or other bodily secretions of a person infected with Lassa fever. There is no epidemiological evidence supporting airborne spread between humans. Person-to-person transmission occurs in both community and health-care settings, where the virus may be spread by contaminated medical equipment, such as re-used needles. Sexual transmission of Lassa virus has been reported”. The disease is

endemic in the rodent population in parts of West Africa (Ogbu *et al.*, 2007; Yun and Walker, 2012; Asogun *et al.*, 2012; Dongo *et al.*, 2013 WHO, 2016). There; has been cases of Person-to-person infections and laboratory transmission can also occur, particularly in the hospital environment in the absence of adequate infection control measures. Accessibility to laboratory diagnosis and prompt treatment are essential [1-5].

The incubation period of Lassa fever ranges from 6–21 days. The onset of the disease, when it is symptomatic, is usually gradual, starting with fever, general weakness, and malaise. After a few days, headache, sore throat, muscle pain, chest pain, nausea, vomiting, diarrhoea, cough, and abdominal pain may follow. In severe cases facial swelling, fluid in the lung cavity, bleeding from the mouth, nose, vagina or gastrointestinal tract and low blood pressure may develop [1-5]. In Lassa virus infection there could be proteinuria. Shock, seizures, tremor, disorientation, and coma may be seen in the later stages. Deafness occurs in 25% of patients who survive the disease. In half of these cases, hearing returns partially after 1-3 months. Transient hair loss and gait disturbance may occur during recovery [1-4].

Death usually occurs within 14 days of onset in fatal cases. The disease is especially severe in late pregnancy, with maternal death and/or fetal loss occurring in more than 80% of cases during the third trimester [1-5].

According to WHO (2016): Lassa fever is known to be endemic in Benin, Ghana, Guinea, Liberia, Mali, Sierra Leone, and Nigeria, but probably exists in other West African countries as well. The overall case-fatality rate is 1%. Observed case-fatality rate among patients hospitalized with severe cases of Lassa fever is 15%. Early supportive care with rehydration and symptomatic treatment improves survival. Though first described in the 1950s, the virus causing Lassa disease was not identified until 1969. The virus is a single-stranded RNA virus belonging to the virus family *Arenaviridae*. About 80% of people who become infected with Lassa virus have no symptoms. 1 in 5 infections result in severe disease, where the virus affects several organs such as the liver, spleen and kidneys. Because the clinical course of the disease is so variable, detection of the disease in affected patients has been difficult. When presence of the disease is confirmed in a community, however, prompt isolation of affected patients, good infection prevention and control practices, and rigorous contact tracing can stop outbreaks[1-4].

WHO (2016) reported that "Lassa fever is known to be endemic in Benin (where it was diagnosed for the first time in November 2014), Ghana (diagnosed for the first time in October 2011), Guinea, Liberia, Mali (diagnosed for the first time in February 2009), Sierra Leone, and Nigeria, but probably exists in other West African countries as well". Lassa fever occurs in all age groups and both sexes. Persons at greatest risk are those living in rural areas where *Mastomys* are usually found, especially in communities with poor sanitation or crowded living conditions. Health workers are at risk if caring for Lassa fever patients in the absence of proper barrier nursing and infection prevention and control practices[1-5]. Because the symptoms of Lassa fever are so varied and non-specific, clinical diagnosis is often difficult, especially early in the course of the disease. Lassa fever is difficult to distinguish from other viral haemorrhagic fevers such as Ebola virus disease as well as other diseases that cause fever, including malaria, shigellosis, typhoid fever and yellow fever [1-4].

Definitive diagnosis requires testing that is available only in reference laboratories. Laboratory specimens may be hazardous and must be handled with extreme care. Lassa virus infections can only be diagnosed definitively in the laboratory using the following tests:

- reverse transcriptase polymerase chain reaction (RT-PCR) assay- gold standard
- antibody enzyme-linked immunosorbent assay (ELISA)
- antigen detection tests
- virus isolation by cell culture.

There is currently no vaccine that protects against Lassa fever[5].

## MATERIALS AND METHODS

### Study Area

#### Nigeria

The Federal Republic of Nigeria commonly referred to as Nigeria, is a federal republic in West Africa, bordering Benin

in the west, Chad and Cameroon in the east, and Niger in the north. Its coast in the south lies on the Gulf of Guinea in the Atlantic Ocean. It comprises 36 states and the Federal Capital Territory, where the capital, Abuja is located. Nigeria is officially a democratic secular country.

Modern-day Nigeria has been the site of numerous kingdoms and tribal states over the millennia. The modern state originated from British colonial rule beginning in the 19th century, and the merging of the Southern Nigeria Protectorate and Northern Nigeria Protectorate in 1914. The British set up administrative and legal structures whilst practising indirect rule through traditional chiefdoms. Nigeria became a formally independent federation in 1960, and plunged into a civil war from 1967 to 1970. It has since alternated between democratically elected civilian governments and military dictatorships, until it achieved a stable democracy in 1999, with the 2011 presidential elections considered the first to be reasonably free and fair.

Nigeria is often referred to as the "Giant of Africa", owing to its large population and economy. With approximately 188 million inhabitants, Nigeria is the most populous country in Africa and the seventh most populous country in the world. Nigeria has one of the largest populations of youth in the world. The country is viewed as a multinational state, as it is inhabited by over 500 ethnic groups, of which the three largest are the Hausa, Igbo and Yoruba; these ethnic groups speak over 500 different languages, and are identified with wide variety of cultures. The official language is English. Nigeria is divided roughly in half between Christians, who live mostly in the southern part of the country, and Muslims in the northern part. A minority of the population practise religions indigenous to Nigeria, such as those native to the Igbo and Yoruba ethnicities.

As of 2015, Nigeria is the world's 20th largest economy, worth more than \$500 billion and \$1 trillion in terms of nominal GDP and purchasing power parity respectively. It overtook South Africa to become Africa's largest economy in 2014. The 2013 debt-to-GDP ratio was 11 percent. Nigeria is considered to be an emerging market by the World Bank; it has been identified as a regional power on the African continent, a middle power in international affairs, and has also been identified as an emerging global power. Nigeria is a member of the MINT group of countries, which are widely seen as the globe's next "BRIC-like" economies. It is also listed among the "Next Eleven" economies set to become among the biggest in the world. Nigeria is a founding member of the African Union and a member of many other international organizations, including the United Nations, the Commonwealth of Nations and OPEC.

### Methods of Data Collection

1. Reports from Federal and States Ministry of Health, Nigeria on internet social media/website.
2. World Health Organization websites

## RESULTS

### Outbreak of Lassa fever in Nigeria

Lassa fever which has afflicted over 284 has killed about 154 Nigerians from different parts of the country from August 2015 to date. Fresh cases have been recorded every day in some states like Ondo and Bauchi, where the outbreak had earlier stopped, signalling that the disease could spread further.

Notwithstanding, Lassa fever outbreak is yet to become an epidemic but there are fears that the continued deaths of Nigerians as a result of the fever may be pointing in a different direction[6]. Five persons have so far been diagnosed with the disease in Ondo state including two cases recorded in Owo Local Government Area and two in Akoko North-West Local Government Area in addition to the case of the student of the Achievers University, Owo-Nigeria who was earlier diagnosed with the disease [7].

Currently, the likely risk for medical personnel is the newest security threat confronting Nigeria. The latest Lassa fever outbreak affected 24 states in Nigeria. Unlike outbreaks of the past, it is spreading in rural and urban areas. In the country today, millions of people are walking around with high fevers and other kinds of symptoms that could confuse diagnosis of Lassa fever. This time, even health workers are not spared. WHO updates Update on the World Health Organisation, WHO, website showed that between August 2015 and 17 May 2016, WHO has been notified of 273 cases of Lassa fever, including 149 deaths in Nigeria. Of these, 165 cases and 89 deaths have been confirmed through laboratory testing (CFR: 53.9 percent). The cases were reported from 23 states. Since August 2015, 10 health care workers (HCW) have been infected with Lassa virus, of which two have died. Of these ten cases, four were nosocomial infections. Just two weeks ago, two medical doctors died from the disease in Anambra and Delta States. As of 17 May 2016, eight states reported Lassa fever cases (suspected, probable, and confirmed), deaths and/or following of contacts for the maximum 21-day incubation period. Currently, 248 contacts are being followed up in the country. The other 15 previously affected states have completed the 42-day period following last known possible transmission [5,8].

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Borno state in northeast Nigeria has recorded its first Lassa fever outbreak in a middle-aged woman from Zabramarri village near Maiduguri was the first confirmed outbreak of Lassa fever in Borno State in since 1969 [8,9].

In order to contain the outbreak, the WHO emergency humanitarian health team in the state has taken a number of actions. This includes rapid training on clinical case management, contact tracing, mobilizing a network of healthcare workers at the hospital, and building public awareness[8].

Nigeria recorded the largest outbreak of Lassa fever in its history between 2015 and 2016, with 273 reported cases

resulting to 149 deaths, the Nigeria Centre for Disease Control, [6] One case of Lassa Fever has been confirmed in Angwan Kura Community, in the old market area of Lokoja, Kogi state capital (Kogi State Ministry of Health, 2017). First death as a result of Lassa Fever disease was recorded in Cross River State [8]. No fewer than eight people have so far died following the recent outbreak of Lassa fever in Nasarawa state [8].

Plateau state reported four deaths, while laboratory tests confirmed five cases of Lassa fever since December 2016 [8]. In Ogun State 396 people that had primary and secondary contacts with the Assistant Chief Nursing Officer of Federal Medical Centre (FMC) Idi- Aba in Abeokuta, who died of Lassa fever have been traced and placed under surveillance [8] The United Nations Children's Fund,(UNICEF), has began an enlightenment campaign of Lassa fever in Anambra state after the recent outbreak of the deadly disease that claimed three lives including a medical doctor [6]. Five more cases of Lassa Fever have been reported in four states in Nigeria, increasing chances that the disease could spread further. Confirming the new cases, Nigeria Centre for Disease Control (NCDC) said that two cases were reported from Plateau State, one from Rivers, and one each from Bauchi and Gombe[6].

A doctor has reportedly died of Lassa Fever in a fresh case of the outbreak of the virus in Asaba, Delta state [6]. A recent outbreak of Lassa fever have killed one medical doctor and three others in Anambra state (Anambra state Ministry of Health).

Lassa fever has claimed 14 lives in Taraba State from January to date, 49 suspected cases of the disease reported in the hospital, 21 persons were treated and discharged (Federal Medical Centre (FMC)[6]. The Lassa fever outbreak in the country has now killed 101 people. Nigeria Centre for Disease Control (NCDC, 2016) statistics showed that reported cases of the hemorrhagic disease confirmed and suspected stood at 175 with a total of 101 deaths. Jigawa State Government has confirmed the death of one person as a result of Lassa fever outbreak in the state[6].

A nursing student in one private nursing school in Nkpor, Idemili North was killed by Lassa Fever, while 65 others are under surveillance [6]. Kano State Government has confirmed 20 fresh cases of Cerebral Spinal Meningitis (CSM) in eight local government councils and two fresh cases of Lassa fever [10].

#### **Public health response with respect to Laboratory Diagnosis**

Currently, two national laboratories are supporting the laboratory confirmation of Lassa fever cases by polymerase chain reaction (PCR) tests. All the samples were also tested for Ebola, Dengue, Yellow fever and so far have tested negative. The two laboratories that are currently operational are:

- Virology laboratory, Lagos University Teaching Hospital
- Lassa fever research and control centre, Irrua specialist hospital

Along with other key partners, WHO is supporting ministry of health in surveillance and response of Lassa fever outbreaks including contacts tracing, follow up and community mobilization. One of a concern since the onset of Lassa fever outbreaks is the high proportion of deaths among the cases that is still under investigation[5]. According to Lassa Fever Control Committee (2017)the outbreak was an emergency,

adding that poor disease surveillance system has caused the escalation and persistent re-occurrence. No fewer than three people are diagnosed of the disease daily in the latest outbreak.

Nigeria abandon disease surveillance and control activities; there was a time people worked together, the laboratories at Ibadan, the Ministry of Health, Nigeria Institute Medical Research, joined forces to protect the country. In the 60s to 80s at Ibadan, they produced every reagent needed in the country. Which does not depend on importation? But now due to laziness and everybody wants to make money from importation Nigeria over depend on importation of reagents [6].

Sadly, with the new trend of the infectious disease, only few Nigeria laboratories can give accurate results. Six to seven laboratories in the country cannot give proper results due to lack of support [6]. The only few that function in the country have the support of partner agencies and backing from abroad [6] Lassa as an annual recurrent budget of death for poor people of Nigeria because Nigeria have lived in a state of denial of the disease and handle it with characteristic laxity, laissez-faire, negligence, sloppiness, slackness, disregard, triviality and freewheeling abandon. "Lassa lacks the zeal and trepidation that Ebola outbreak inspired and Nigeria still wakes up every year an outbreak is reported, "running like a decapitated chicken in any which direction, and forgetting about the disease till another year another outbreak".

Currently, two national laboratories are supporting the laboratory confirmation of Lassa cases by polymerase chain reaction (PCR) tests. All the samples were also tested for Ebola, Dengue, Yellow fever and so far have tested negative. The two laboratories that are currently operational are Virology laboratory, Lagos University Teaching Hospital and Lassa fever research and control centre, Irrua specialist hospital, Nigeria/Lahor Research Laboratory. Along with other key partners, WHO is supporting the Federal Ministry of Health, Nigeria in surveillance and response of Lassa outbreaks including contacts tracing, follow up and community mobilization[5].

A study in the journal Cell by a team that included Christian Happi of Irrua Specialist Hospital-where experts confirm strains of Lassa fever in samples had traced "ancient roots" of Lassa nearly 1,000 years to a region that is now present-day Nigeria. Up till 2008, specimens were flown abroad for confirmation. Since 2008, two centres have stepped in to fill the gap in laboratory diagnosis and research into the fever-Lassa Fever Research and Control Centre at Irrua Specialist Hospital, Edo, and Lahor Research. Samples from the latest outbreaks have undergone confirmation at Irrua, which also provided confirmation for cases from 2012 onwards. In 2012, the number of cases peaked in 2012, when 1,723 cases with 112 fatalities were recorded. In 2012, half a million vials of Ribavirin, an antiviral drug considered effective were procured after the first case of Lassa was reported in Ebonyi. By then, one doctor and up to four nurses had died, some others were hospitalised at Federal Teaching Hospital, Abakiliki. Lassa fever has the greatest impact among haemorrhagic fevers-rivalled only by dengue. Up to 300,000 are infected annually in West Africa alone, and an estimated 5,000 of them die. During 2012 and 2013, more than 2900 cases were reported in widespread outbreaks that occurred across many states. In 2013, three deaths-among them a health worker, it struck in

Benue and Ondo States. Since the last quarter of 2015, the country has been battling the epidemic disorder, which at the last count, has reached 24 states and killed 154 people. More than 684 suspected cases have so far been recorded in the Borno, Gombe, Yobe, Taraba, Plateau, Nasarawa, Ebonyi, Edo, Ondo, Rivers, Bauchi, Anambra, Lagos, Niger, Kano, Nassarawa, Plateau, Oyo, Gombe and Ondo, Kano states and the FCT amongst others and still counting [8].

### Findings

Cases of Lassa virus infection have been reported in 24 of the 36 states in Nigeria with only 2 diagnostic and confirmatory Laboratories located in only two geopolitical zone of the six zones in Nigeria which include: South- South and South-West. Cases are still being reported in Nigeria up till this present moment of June, 2017.

The number of the Laboratories is not enough to cope with the need for a thorough surveillance for qualitative healthcare as many cases will escape unreported. There is no accessible Diagnostic Laboratory for screening in many states and local governments in Nigeria. The current data may not be the accurate pattern of occurrence in Nigeria

Students and National Youth Corps are involved in the current cases reported which is a threat to Public Health. These set of Nigerians cohabit with many others over a period of time and later leave for larger society. Awareness of the spread of lassa fever is not enough compared with that of HIV/AIDS.

### CONCLUSION

The scourge of lassa fever is becoming endemic in 24 states of Nigeria possibly due to inadequate access to Lassa fever testing Laboratories. The spread does not discriminate gender, age and economic status. Students and National Youth Corps who cohabit with many others over a period of time and later leave for larger society are also affected which could greatly increase the spread.

### Recommendations

1. Establishment of Lassa virus screening laboratories in Private and Public academic tertiary institutions
2. Establishment of Lassa virus confirmatory laboratories in Private and Public secondary and tertiary health institutions
3. Aggressive and massive public health education
4. Restructuring of Nigeria Centre for Disease Control to include reasonable number of Medical Laboratory Scientists/Virologists
5. Adequate fund allocation and release to Public Health issues
6. Establishment of Diagnostic Laboratories in all Primary Health Care Centers
7. Appointment of more Medical Laboratory experts
8. Sponsorship of Clinicians and Medical Laboratory Scientists for special training in the diagnosis of infectious diseases.

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