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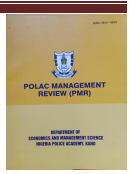

EMERGING/RE-EMERGING INFECTIOUS DISEASES: THE CASE OF LASSA FEVER IN NIGERIA

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Abstract

The study examined the emerging of Lassa fever infectious disease in Nigeria which started in 1969. The study discusses the current state of Lassa fever in Nigeria and its emergence as a public health concern. It also delves into the epidemiology, transmission, and clinical presentation of Lassa fever, as well as the challenges and strategies for its prevention and control in Nigeria. This study serves as a valuable resource for researchers and public health professionals interested in understanding and addressing the issue of Lassa fever in Nigeria. The need for advocacy on ways of preventing spread and further outbreaks as well as proper treatment and handling patients of Lassa fever to health workers and those at risk can also never be overemphasised.

Keywords: Infectous, Disease, Lessa, Fever

Introduction

An Emerging or Re-emerging Disease is the emergence of a pathogen in human or animal population which is related to the increase in distribution, increase in incidence, increase in virulence or increase in other factors (Jones et al, 2008). The Centre for Disease Control and Prevention (CDC, 2007), has it that, an emerging infectious disease is one whose incidence in humans has increased in the past 2 decades or threatens to increase in the near future. These diseases respect no national boundaries and include:

i. New infections resulting from changes or evolution of existing organisms
ii. Known infections spreading to new geographic areas of populations
iii. Previously unrecognised infections appearing in areas undergoing ecologic transformation
iv. Old infections re-emerging as a result of antimicrobial resistance in known agents or breakdown in public health measures

According to Turkson (2011), an Emerging Disease covers any one of these 3 situations:

i. a known agent which appears in a new geographic area
ii. a known agent or its close relative which occurs in a hitherto unsusceptible species
iii. a previously unknown agent which is detected for the first time

According to Climate Change and Health Initiative (CCHI, 2008) at least a new disease has emerged on an average of every 7 months since 1980 and there have been about 335 emerging infectious diseases between 1940 and 2004 with more than 50% of these infections caused by bacteria/rickettsia. There are several diseases therefore that can be said to have met all the criteria to be described as emerging/re-emerging infectious diseases in Nigeria. Among the several of these diseases is the Lassa fever.

Lassa fever is an acute viral heamorrhagic fever that is caused by a rodent borne arenavirus which is endemic in West Africa (Harper, 2004; Wolfe, 2008). Lassa fever was first discovered in Sierra Leone in the 1950s (Ogbu et al, 2007) but the Lassa virus was first described/identified in 1969 in the town of Lassa, in Borno State, Nigeria in the Yedseram river valley at the south end of Lake Chad (Frame et al, 1970) when two missionary nurses died. The man behind this discovery was John Davidson Frame who was a missionary doctor and died on 16th January, 2008 at the age of 90 years having been born in 1917 in Iran where his father also John Frame was a

protestant missionary and chief physician at the American Hospital (Miller, 2008).

Lassa fever which has symptoms such as fever, muscle aches, sore throat, nausea, vomiting, chest and abdominal pains among others, appear to have re-emerged and reports in February 2012 made mention of outbreaks of the disease in Nigeria which killed 40 people in 12 states across the country (Ahmadu-Suka, 2012; Sylvester, 2012). These States are Borno, Gombe, Yobe, Taraba, Plateau, Nasarawa, Ebonyi, Edo, Ondo, Rivers, Anambra and Lagos. The mortality rate of the disease was up to 20% within just weeks of being noticed.

The emergence/re-emergence of this highly virulent and contagious Lassa virus in many more communities and states in our country and the increasing sporadic cases of Lassa fever even outside areas hitherto known for the disease due to inter-border traffic and travels, bring out the need for stakeholders and indeed the entire Nigerians to have handy comprehensive information about the virus and the Lassa fever itself. This information, if available will be of paramount importance in implementing appropriate barriers and nursing guidelines not only to institutions but to individuals and therefore act as checks and balances for further spread of the disease. The aim of the study is therefore to raise alarm and so create the needed awareness as to the re-emergence of this deadly Lassa fever. The overview of this disease in areas such as epidemiology, clinical presentation/symptoms, vector, treatment, prevention and control and provision of such other necessary information should be able to tame the deadly tide of the effects of Lassa fever.

Other objectives of the study are to:
i. Provide policy options to Government that can further help in controlling the spread of the disease
ii. Propagate sanitary and other preventive measures necessary for the mitigation of the disease and to
iii. Conclude if Government's effort at fighting the deadly disease is adequate or not and what needs to be done now and in the future in fighting the disease.

Literature Review

Conceptual Issues

According to National Institute of Allergy and Infectious Disease (NIAID, 2022), Emerging Infectious Disease (EID) is an infectious disease that has newly appeared or has existed but is rapidly increasing in incidence of geographic range. McAthur (2020) simply puts it as new infections resulting from changes or evolution of existing organisms, known infections spreading to new geographic areas or populations, previously unrecognised infections appearing in areas undergoing ecologic transformation, or old infections re-emerging because of antimicrobial resistance on known agents or breakdowns in public health measures. EIDs account for at least 15% of all human pathogens with many of them being zoonotic or synoptic which means an animal receptacle incubating the organism with random transmission into human populations. The spread could be airborne, vector borne or foodborne and to be infectious the agent must have the ability to spread from human to human and cause disease.

Theoretical Framework

The theory of Re-emergence of emergence as described by the Institute for the Study of Complex Systems cited by Corning (2015) suffices in the present work. Accordingly, the philosopher David Blitz in his writing titled "*Emergent Evolution: Qualitative Novelty and the Levels of Reality* (1992), the term "emergent" was coined by the pioneer psychologist G. H. Lewes in his multi-volume *Problems of Life and Mind* (1874-1879). Like many post-Darwinian scientists of that period, Lewes viewed the evolution of the human mind as a formidable conundrum. Some evolutionists, like Alfred Russel Wallace (the co-discoverer of natural selection), opted for a dualistic explanation. The mind is the product of a supernatural agency, he claimed. But Lewes, following the lead of the philosopher John Stuart Mill, argued that, to the contrary, certain phenomena in nature produce what he called "qualitative novelty" — material changes that cannot be expressed in simple quantitative terms; they are emergents rather than resultants. From emergent evolution the theory became submergence of emergence in the 1930s all in an attempt to tie

loose ends in the earlier theory. The theory of re-emergence of emergence still asks the question "how does emergence emerge"?

In conclusion, the theory of re-emergence of emergence refers to -the arising of novel and coherent structures, patterns and properties during the process of self-organization in complex systems. The theory has common characteristics as follows: (1) radical novelty (features not previously observed in the system); (2) coherence or correlation (meaning integrated wholes that maintain themselves over some period of time); (3) A global or macro "level" (i.e., there is some property of "wholeness"); (4) it is the product of a dynamical process (it evolves); and (5) it is "ostensive" — it can be perceived. Unfortunately, this appears to be the characteristics of Lassa fever and has therefore assumed the position of an emerging/re-emerging infectious disease in Nigeria.

Factors Contributing to Emergence/Re Emergence of Diseases

According to Turkson (2011), the factors that contribute to emergence/re-emergence of diseases are genetic, biological, social, political and economic which include the following:

i. Microbial adaptation and change
ii. Human susceptibility to infection
iii. Climate and weather
iv. Changing ecosystems
v. Human demography and behaviour
vi. Economic development and land use
vii. Technology and industry
viii. Breakdown of public health measures
ix. Poverty and social inequality
x. War and famine
xi. Lack of political will
xii. Intent to harm (Bioterrorism/Bio-warfare)
xiii. Altered landscape (bringing hosts into contact with new pathogens)
xiv. Greater population densities (facilitating rapid spread)
xv. Faster, longer-distance travel and trade (carrying diseases to new populations)
xvi. Natural disaster or war (disrupting ability to keep diseases in check)
xvii. Climate change of natural or anthropogenic origin (being a driver to changes in disease dynamics)

Historical Account of Lassa Fever

Lassa Virus was first described in the 1950's in Sierra Leone but identified in 1969 when two Missionary Nurses died in Nigeria; Lassa virus was named after the town in Nigeria where the first cases were isolated. Since then, a number of outbreaks of Lassa virus infection have been reported in many parts of Nigeria including Jos, Onitsha, Zonkwa, Abo Mbaise, Owerri, Ekpoma and Lafia (Ogbu et al, 2007). There are also cases of importation of the virus into other parts of the world (Table 1). Out of the 24 cases of imported Lassa virus from West Africa, 9(37.5%) of these came from Nigeria and 7(29%) of these cases ended up in death. Some earlier reports have however recorded fatality rate of up to 65% (Fisher-Hoch, et al; 1995). Out of Ten admitted cases of Lassa fever of health care workers from 2005 – 2008, seven of those cases ended up dying, showing a high mortality rate associated with the disease (Table 2).

Table 1: Worldwide cases of imported Lassa fever (1969-2004)

S/no	Year of Import	From	To	Occupation	Outcome
1	1969	Nigeria	USA	Nurse	Survived
2	1971	S/Leone	UK	"	"
3	"	"	"	Physician	"
4	1972	"	"	Nurse	"
5	1974	Nigeria	Germany	Physician	"
6	1975	"	UK	"	Died
7	"	S/Leone	USA	Aid Worker	Survived
8	1976	"	"	"	"
9	"	Nigeria	UK	Engineer	"

10	1980	Upper Volta	Netherlands	Aid Worker	"
11	1981	Nigeria	UK	Teacher	"
12	1982	"	"	Diplomat	"
13	1984	S/Leone	"	Geologist	"
14	1985	"	"	Nurse	"
15	1987	SLeone/Liberia	Isreal	Engineer	"
16	"	S/Leone	Japan	"	"
17	1989	Nigeria	Canada	Agric Specialist	"
18	"	"	USA	Engineer	Died
19	2000	Cote d'Ivoire/B Faso/Ghana S/Leone	Germany	Student	"
20	"	Nigeria	UK	Peacekeeper	"
21	"	S/Leone	Germany	Unknown	"
22	"	S/Leone	Netherlands	Physician	"
23	2003	SLeone/Liberia	UK	Peacekeeper	Survived
24	2004		"	Businessman	Died

Source: Wolfe, 2006

Table 2: Outcome of some cases of Lassa fever in Nigeria (2005-2008)

Locality/hosp	Case no.	Date of adm.	Age/sex	Outcome	HCW
Abakiliki, Ebonyi State (EBSUTH)	1	04/02/05	40/M	Survived	Nurse
	2	07/02/05	54/F	Died, Feb 13	Nurse/contact to case 1
	3	21/02/05	35/F	Survived	Nurse/contact to case 2
	4	21/02/05	36/F	Died, Mar 1	Nurse/contact to case 2
	5	17/01/08	38/M	Died, Jan 23	Doctor
	6	05/03/08	38/M	Died, Mar 11	Doctor
Abuja, FCT (NHA)	7	02/01/08	37/M	Died, Jan 7	-
Jos, Plateau State	8	Dec/07	19/M	Died	NA
	9	Feb/08	30/M	Died	-
	10	Feb/08	28/M	Survived	-

Source: Ehichioya et al, 2010

In February 2012, Lassa fever outbreak in Nigeria as reported by Nigerian Media was in 12 States with 87 confirmed cases and 40 deaths as at 17th February 2012. The States were Borno, Gombe, Yobe, Taraba, Plateau, Nasarawa, Ebonyi, Edo, Ondo, Rivers, Anambra and Lagos. The FCT had 3 reported cases but without any confirmed death (Daily Trust, Feb. 29,2012, p viii; Mar 5, 2012, p 38). The Federal Government of Nigeria responded by distributing Lassa Fever vaccines/drugs and inaugurating a Lassa Fever Rapid Response Committee to prevent and control further outbreak of the disease. The Federal Government procured and 500,000 vials of ribavirin drugs and distributed to the affected states

Ten years later, from January 3 to January 30, 2022, alone, there have been reported outbreaks in 14 states with 211 confirmed laboratory tests, 40 deaths and case fatality ratio of 19% (WHO, 2022). The details show that three states accounted for 82% of confirmed cases as follows: Ondo (63), Edo (57) and Bauchi (53). Other states affected were Benue (11), Ebonyi (5),

Oyo (5), Taraba (5), Kogi (4), Enugu (2), Kaduna (2), Cross River (1), Delta (1), Katsina (1) and Plateau (1)). These reoccurrences over the years are a sign that Lassa fever is a emerging/re-emerging infectious disease in Nigeria.

According to WHO (2023) as at April 2023 alone, Nigeria experienced a large outbreak of Lassa fever, with 4702 suspected cases, 5 probable cases, and 877 confirmed cases and 152 case fatality rate (i.e. CFR 17%)

Rodent Species as Vector

Out of the 4000 species of mammals, 1700 are rodents (FAO, 2012). Among the rodents, the family Muridae and genus Rattus contain the most species. The genus Rattus has 3 species found throughout the world; they are house mouse (*Mus musculus*), house or roof rat (*Rattus rattus*) and the brown rat (*R. Norvegicus*). Other rat species in the same genus such as multimmate rat (*Promys (Mystomys) nalalensis*) and spiny mouse (*Acomys cahirinus*) are found only in Africa; while the Pacific rat (*R. Exulans*), the bandicoot rat (*Bandicota bengalensis*) are found in Asia (FAO, 2012).

Lassa virus is zoonotic, meaning it is transmitted from animals. Specifically, Lassa virus is spread to man from rodents, particularly from the multi-mammate rat called *Mastomys natalensis. M. natalensis* is probably the most common rodent in equatorial Africa, it is also ubiquitous in human households and eaten as a delicacy in some areas (Ehichioya et al, 2012).
Mystomys natalensis is economically the most important rodent pest in Africa and a true indigenous commensal, in some areas it is replaced by the much larger *R. rattus*. The fur is soft, brownish on the back and greyish underneath. The head + body is up to 150 mm and the fully grown adult is about 50-100g by weight. The tail, which is uniformly dark is about the same length as the head + body (appendix 1).

Epidemiology and Pathogenesis

Lassa fever is endemic in West Africa; it has been reported in Sierra Leone, Congo, Guinea, Liberia, Mali, Senegal and Nigeria with studies indicating that 300,000 – 500,000 case and 5,000 deaths occurring yearly in the entire West Africa (Carey, et al, 1972; Monath, et al, 1974; WHO, 2005; Wikipedia, 2012). Since 1969, there have been a number of outbreaks of the disease and reported in different places including Jos (Plateau), Onitsha, Zonkwa (Kaduna), Abo Mbaise and Owerri (Imo), Ekpoma (Edo) and Lafia (Nasarawa) (Fisher-Hoch et al, 1995; FMH, 2000). A few other cases have been reported outside West Africa but this has usually been due to importation by travellers into USA, Canada, United Kingdom, Germany, Netherlands and Israel (Wolfe, 2006)

Cases of Lassa fever outbreaks are usually not depended on seasons; however, there are more cases during the rainy seasons than the dry seasons. The outbreak that is most recent in Nigeria was that of early February, 2012. However, in the times when there are no outbreaks, there are evidences of Lassa virus activities. For example, 10 cases of Lassa fever were confirmed by virus detection or implicated by epidemiologic investigation and serologic testing between 2005 – 2008 (Table 2) in Edo, Ebonyi, Anambra, Plateau States and the FCT (Ehichioya *et al*, 2010).

The prevalence of Lassa virus antibodies in Nigerians is highest with rates of over 20%, for other countries the ranges are: Guinea -7%, Sierra Leone and Liberia - 15-20% (Bloch, 1978; McCormick et al, 1987). About 15-20% of patients admitted in hospitals/clinics for the disease usually die of the illness but 80% of these same human infections are mild or asymptomatic.

The Lassa virus is harboured by the rodents' species *Mastomys natalensis*. Infected rodents remain carriers throughout their life and show no clinical symptoms but excrete the virus through their urine, saliva, respiratory secretion and exposed blood vessels. This way, humans become infected through contact with these substances. The transmission to man is through faecal-oral route or the respiratory track through inhalation of contaminated air containing the virus or even when infected blood touch bruised skin or by sexual intercourse (McCormick, 1987). This means that infected individuals constitute a serious threat to the environment.

Lassa fever occurs in male and female and in all age groups without bias but those at greater risks are

persons living in rural areas where the rodent *M. natalensis* is usually found and in places of poor sanitation or crowded living conditions. About two third of all reported cases are women but this may be as a result of exposure rather than a tendency of greater susceptibility in women to the disease (Harper, 2004). Health care workers are also at high risk if proper barrier nursing and infection control are not maintained.

Symptoms/Clinical Presentation

The symptoms of Lassa fever are difficult to be distinguished from diseases such as severe malaria, typhoid fever, yellow fever and other viral heamorrhagic fevers like Marburg and Ebola (Ogbu, et al 2007; Wikipedia, 2012). After the incubation period which is usually between 3-21 days, there is an acute illness with multi-organ involvement and non-specific symptoms that include fever, facial swellings, muscle fatigue, conjunctivitis and mucosal bleeding. Lassa virus can infect almost every tissue in human body, it usually starts with the mucosa, intestine, lungs and urinary system then progresses to the vascular system (Wikipedia, 2012). Other symptoms arising from the following affected organs are:

1. Gastrointestinal tract
   i. Nausea
   ii. Vomiting (bloody)
   iii. Diarrhoea (bloody)
   iv. Stomach ache
   v. Constipation
   vi. Dysphagia (difficulty swallowing)
   vii. Hepatitis

2. Cardiovascular system
   i. Pericardiatis
   ii. Hypertension
   iii. Hypotension
   iv. Tachycardia (abnormal high heart rate)

3. Respiratory tract
   i. Cough
   ii. Chest pain
   iii. Dyspnoea (breathing difficulty)
   iv. Phyryngitis
   v. Pleuritis

4. Nervous system
   i. Encephalitis
   ii. Meningitis
   iii. Unilateral of bilateral hearing deficit
   iv. Seizures

Diagnosis and Treatment

Clinical diagnosis of Lassa fever is difficult especially early in the course of infection. As a result, clinical manifestation, epidemiological data and laboratory findings are all taken into consideration for diagnosis. Laboratory diagnosis is by isolation of Lassa antigen, antibodies using virus isolation techniques. The virus can be isolated using laboratory animals such as Albino Mice, Guinea Pigs, Vero Cell and African Green Monkeys (Ogbu, 2007).

Ribavirin is the antiviral drug used against Lassa fever but it must be used for treatment early in the course of the illness. Ribavarin used in the first six days of infection had a case-fatality-rate (CFR) of 5% compared to another study which had CFR of 26% when the drug was administered from 7 days onward after the onset of the fever (McCormick *et al*, 1986). Supportive treatment is necessary and includes fluid replacement, blood transfusion, and administration of paracetamol, phylometadione, ringer lactate, haemocoel quinine and broad spectrum antibiotics (Holmes *et al*, 1990).

Prevention and Control

Prevention of primary transmission of Lassa virus from its host to humans should be achieved by avoiding contact with Mastomys rodents. Notice of damage and burrows are some of the several ways that signal the presence of rodents in homes. Footprints in dusty places, scattered droppings and smears are some of the other signals of the presence of rodents. Care must however be taken, because these signs mentioned above are only apparent after a substantial population has become well established (FAO, 2012). The subtle sign of a rat just passing through in the house is sufficient. Foods must be put away in rodent-proof containers and homes kept clean to discourage rodents from entering homes. It may not be wise to use these

rodents as foods as practiced in some parts of the country.

As a result of the fact that Lassa haemorrhagic fever is highly contagious, further transmission from person-to-person contact or nosocomial routes must be avoided by preventing contacts with patient secretions (i.e. instituting strict barrier nursing). The restrictions include wearing protective clothing such as masks, gloves, gowns and goggles; using infection control measures such as complete equipment sterilisation and isolating infected patients from contact with unprotected persons until the full course of the disease has been run (Fisher-Hoch et al, 1995).

Materials such as body fluids, excreta and others of the patient should be handled carefully and disposed properly preferably by burning. Other instruments used on the patient if not disposable must be subjected to autoclaving immediately. Care must be taken when collecting, transporting and carrying out bacteriological/biochemical investigations on pathological materials in laboratory. Those who have had contact with suspected Lassa haemorrhagic fever patients must be traced, monitored with specimens collected for laboratory diagnosis and those found positive must be isolated and treatment started as soon as possible with ribavirin.

Conclusion and Recommendations

The Federal Government must have in mind the possibility of periodic outbreaks of Lassa fever in Nigeria and should therefore not shy away from the establishment of well-equipped diagnostic/research facilities that should provide rapid molecular testing at referral centres in each of the disease endemic zones. The testing in this referral centres will facilitate appropriate case and contact management, including early treatment and post exposure prophylaxis as already mentioned.

The Federal Government through the Federal Ministry of Health should ensure that Ribavirin the drug for the treatment of Lassa fever is constantly made available in hospitals/clinics particularly in the rural communities of the endemic areas. This should be against the usual "fire-brigade" attitude of purchasing and supplying the drug to the States only when and where there are reported outbreaks.

Advocacy on health education strategies of ways of preventing spread of infection to people living in endemic areas must be instituted and should measure particularly on ways of controlling or minimising contact with rodent excreta. Emphasis should also be made on methods to control virus transmission from infected patients such as precautionary measures, isolation of suspected cases and surveillance of contacts.

This paper concludes by saying that, getting rid of all forms of rodents in the house appear to be the best way of prevention from Lassa fever (No law in Nigeria protects rats). This is to say that, the price of the practice of modern medicine in cases of Lassa fever which include treatment that could still lead to death is far more too high a pay than the price of good sanitary/medical practice.

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