The Existence of Rift Valley Fever Virus in Nigeria: Past, Present, And Future

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Abstract

Over 90 years ago, precisely in 1931, Rift Valley fever (RVF) was discovered in Kenya. However, the virus spread to African countries including Sudan, Somalia, South Africa, Madagascar, Egypt, and Tanzania. It also spread to Saudi Arabia and Yemen. Rift Valley fever is an arthropod-borne viral zoonotic disease affecting various species of animals such as cattle, goats, sheep, camels, wild animals, and even humans. It is a highly infectious and contagious disease with quickly spread to other countries through the borders or international movements of animals. RVF is highly economical and of public health significance because it causes neonatal death and decreases milk production in animals, and it is associated with hemorrhagic fever, encephalitis, and ocular diseases in humans. Heavy and persistent rainfall, flooding, and availability of mosquito breeding sites such as lakes and water bodies around the animal herd influence the occurrence of RFV because mosquitoes especially *Aedes* and *Culex* serve as the primary vector of the disease. Humans become infected following contact with tissues, fluids, and infected animals. In animals, RVF is characterized by hemorrhagic fever, and abortion, while in humans it is associated with encephalitis, ocular diseases, and hemorrhagic fever. In this review article, we discussed the past and present seroprevalence study of Rift Valley in Nigeria then we forecast and suggested respective ways and methods to follow to prevent the future occurrence of the disease in Nigeria.

Background

Rift Valley fever (RVF) is an acute febrile disease of various species of animals (cattle, sheep, goats, and camels) including humans (zoonotic). The disease is also referred to as enzootic hepatitis of cattle and sheep (Adeyeye *et al.,* 2011). The disease is an arthropod-borne disease caused by Rift Valley fever virus (RVFV) belonging to the family *Bunyaviridae* (Yousif *et al.,* 2014). RVFV belongs to the large group of RNA viruses known as Bunyaviruses that is mainly transmitted by arthropods (Natalia *et al.,* 2020). They are associated with various febrile diseases in both

humans and animals (Robert, 1996). Genetically, the virus is an enveloped RNA virus consisting of three (3) segments L, M, and S, and all the steps involved in its replication happen within the infected cells (Michel *et al.*, 2010). However, studies on how the virus is assembled are difficult to carry out due to biosafety levels (Liu *et al.,* 2008).

RVF was initially identified on a sheep farm in the year 1931 in Kenya (Shope *et al.*, 1982). However, further outbreaks occur in other African countries and few Asian countries. In the year 2000, RVF outbreak was reported in Saudi Arabia and Yemen. Another outbreak was also reported in Egypt in 2003, Kenya, Tanzania, and Somalia in 2006, 2007 in Sudan, Madagascar in 2008 - 2009, the Republic of South Africa in 2010, the Republic of Mauritania in 2012, and a report from the Niger Republic in 2016. These many sightings shows that the virus is highly endemic in Africa.

RVF was first characterized by Daubney *et al*. (1931). The incubation period ranges between 2 to 3 days following infection. In animals, the disease is characterized by increased body temperature (severe fever), abortion, agalactia, and weakness, while in humans it is associated with ocular diseases, encephalitis, and hemorrhagic fever that is characterized by hemoptysis, hematochezia, bleeding from gums, skin, and nose. The disease is highly economical and of public health significance because it causes massive abortions and reduces milk production in ruminants and affects humans as well (Kwaśnik et al., 2021).

RVFV is transmitted mainly via bites of infected mosquitoes particularly *Aedes* and *Culex*, and through the bites of other hematophagous insects, humans become infected when they are in contact with tissues, or body fluid of infected animals (Shabani *et al.,* 2015; Davies *et al.*, 2006; Gerdes, 2004). Veterinarians, laboratories, and other animal health workers are at high risk of infection. Environmental factors particularly flooding and heavy rainfalls lead to the formation of valleys, streams, and lakes which serve as the breeding sites for mosquitoes and support their multiplication.

Different animal models were used in understanding the pathogenesis and pathology of RVF such as mice, rats, hamsters, rhesus monkeys, lamb, adult sheep, and ewe. The studies show that clinical signs differ among infected animals and yet the host factor responsible for causing hemorrhagic fever is not yet identified (Ikegami, and Makino, 2011). The liver serves as the predilection site of the Rift Valley Fever virus (Findlay *et al.*, 1931).

In Nigeria, no case of RVF is reported yet based on the information available to us. However, evidence from serological studies shows that the virus is circulating in different herds and regions in Nigeria. Based on studies conducted in the northern part of Nigeria, antibodies were found in a dromedary camel. Moreover, in the Kaduna and Sokoto states of Nigeria, antibodies were also detected in goats, sheep, and camels (Ezeifeka *et al.,* 1982). Antibodies in animals were also found in

Maiduguri, Katsina, and the Kano state of Nigeria. Based on the epidemiological model, the geographical transfer of the RVFV is a result of host and vector migration between patches (Tianchan *et al.,* 2012).

Based on previous studies conducted on the prevalence of RVFV in some regions of Nigeria, there is little to no research on the determinants that lead to the occurrence of RVFV in Nigeria. Therefore, our present study will address the various determinants that lead to the occurrence of the Rift Valley fever virus in Nigeria.

The occurrence of any infectious disease in the human and animal populations delineates causative agents (which could either be viruses, bacteria, or fungi), the host, and environmental factors. These three determinant influences the occurrence of infectious diseases in a population and are referred to as the epidemiological triad. Infectious diseases only occur when an agent meets a susceptible host in an environment that favors their survival. For the agent, the factors include the type of genotypic change, virulence, and pathogenicity. For the host, are age, sex, species, breed, and nutrition while the environmental factors include geographical location, temperature, and rainfall.

Materials and Methods

We used PubMed, Scopus, and Google scholar to source research articles published from Nigeria on RVF. We used keywords such as ‘Rift Valley Fever’, ‘Rift Valley Fever Virus’, ‘Nigeria’, Africa, etc to search the databases. More than 100 articles were downloaded and later narrowed to 80 articles after proper reading of the content of the articles related to our research question. We categorized our study into past, present, and future based on the number of articles downloaded from 1980 to 2022. We considered work done between 1980 to 2017 as past studies because of paucity of articles published within these years and work done from 2018 to 2022 as present studies.

Environmental Factors

Certain environmental factors are determinants of disease occurrence. Heavy rainfall and low temperature enhance the transmission of RVFV in both human and animal populations. Areas with tragic rainfall and massive flooding will lead to the formation of water bodies such as lakes, valleys, and stagnant water which support the multiplication and hatching of mosquitoes' eggs. The eggs of these mosquitoes usually hatch and last for decades in the environment. Kaduna, Katsina, Kano, Borno, and Sokoto states show the presence of the RVFV in Nigeria based on the serological test (figure 1). In order to understand how animals were exposed to RVFV, the elements of the environment in these regions must be studied.

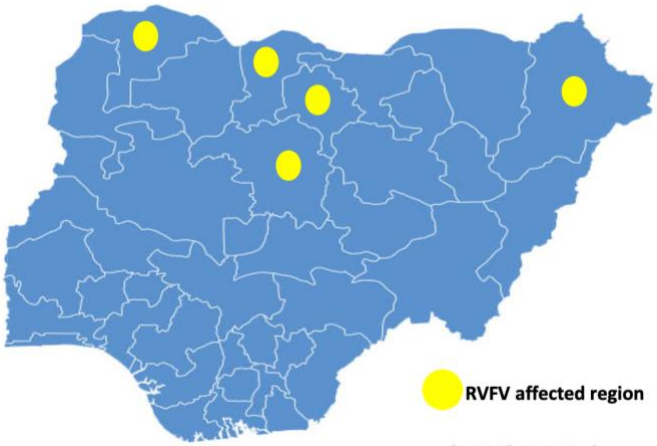

FIGURE 1. Map of Nigeria showing seroprevalence of Rift Valley fever virus (RVFV) in the northern part of Nigeria

Kaduna state is in the Northern Guinea savanna; its climate is regulated by the Sahara high-pressure and Atlantic low-pressure weather system, having a mean monthly temperature of between 26 and 33 degrees Celsius with an average annual rainfall of 1200mm. It lies between latitude 10 and 11 degrees North and longitude 7- and 8 degrees East at an altitude of 645m above sea level (Bununu *et al.*, 2015). Borno state is in the Sahel region of northeast Nigeria, having a mean annual rainfall of 650mm and temperature of 32 degrees Celsius, at latitude 11 05' north and longitude 13 05' east with 3500m above sea level. Katsina state is situated in the Sahel Savannah region of northern Nigeria between latitudes 11007'49N – 13022'57 North and longitude 6052'03E9002'40 East. It has an annual rainfall of 640mm with an average annual temperature of 41 degrees Celsius. Sokoto state is situated at 13.0533° N, and 5.3223° E latitude and longitude respectively. Sokoto states have an annual rainfall of 629mm. An annual average temperature of 28.3 degrees Celsius. Kano state latitude and longitude coordinates are 12.000000, and 8.516667 respectively, with an annual rainfall of 696.4mm and an average temperature of 35 degrees Celsius.

Considering the geographical location and climate of these highlighted states in Nigeria gives the virus the opportunity to propagate very fast and cause an economical threat to the farmers. The increased membrane fluidity and cytoskeletal dynamics brought on by the warmer temperatures in these regions can facilitate the transmission of RVFV, which typically rely on these cellular components for replication and host-cell dissemination (Amari et al., 2021). Therefore, the geographical locations and climate of these regions need to be studied to understand the environmental influence that caused the presence or occurrence of RVF infection in such regions.

Agent Factors

Infectious agents possess certain determinants responsible for inducing damage to the host after infection. These factors could vary with the strain of the virus, and the virus strain could vary with location or geographical region. The most important factor or determinant is virulence, which is the degree of damage or impairment caused by the virus to the susceptible host.

However, the main virulence factor for RVF is a non-structural and multifunctional protein that can inhibit the host's innate immune response (Nicolas *et al.*, 2008). To understand the epidemiology of RVF in Nigeria, the virus needs to be isolated, identified, and characterize in various regions and different species of animals. The strain of the virus or the virulence factor may vary, and it may serve as the major reason why RVF infection is not severe in Nigeria compared to other African countries with the outbreak. Infectious agents undergo genotypic changes such as mutation, conjugation, recombination, and transformation to cause disease in their host.

Host Factors

Host factors that influence the occurrence of infectious diseases in a population differ. It could either be innate or acquired. The host uses different mechanisms to avoid or evade infectious agents during disease transmission, including skin, mucus membranes, secretions (such as mucin and fatty acid that suppress the growth of the infectious agent), and other structures such as keratin, and ciliated cells. Important host factors that are to be considered during the occurrence and transmission of infectious diseases include age, sex, species, previous exposure to the virus, and nutritional and health status. These factors need to be considered in animals that were found to be seropositive based on previous studies in Nigeria to understand the exact factors that influence the occurrence of RVF in Nigeria.

The infectious disease only occurs when all these factors; Environmental, host, and agent are present. To understand the gap in RVFV transmission in Nigeria, these determinants need to be studied. Knowledge of the agent, host, or environmental factors would provide a clue on the actual factor that results in the occurrence of the Rift Valley fever virus in the various region in Nigeria based on past and present studies and we will look at the various ways to prevent its occurrence in the future. Other factors that also play important role in the transmission of diseases in a population include ecological changes, technology, and evolution.

Diagnosis of Rift Valley Fever Virus

Early detection of the disease is very important in providing an effective way of implementing preventive measures. RVFV can be diagnosed based

on the history of the herd such as abortion, neonatal death, or malformations, decreased milk production or agalactia, and hemorrhagic fever that is characterized by bleeding from the body orifice. Clinical signs and laboratory confirmation include, (1) gross pathological lesions mentioned (2) Virus isolation from blood at the acute phase of the disease. Virus isolation can be confirmed by using either immunostaining or reverse-transcription polymerase chain reaction (Karen *et al.*, 2015) (3) Serological tests such as Enzyme-linked immunosorbent assay (ELISA), Haemagglutination inhibition test (HIA), and virus neutralization test can also be used to detect the presence of RVFV (4) Molecular techniques which include RT-PCR, qRT PCR, and Nested RT-PCR (Escadafal *et al.*, 2013). Histopathologically, the following collection of liver tissue hows characteristics of the RVFV and immunostaining reveals specific identification of the Rift Valley fever virus antigen (Karen *et al.*, 2015). RVFV affects various internal organs such as the liver, spleen, lungs, gallbladder, lymph nodes, heart, brain, and gastrointestinal tract, and lesions are produced or seen during post-mortem examination.

Odendaal *et al*. (2020) described the pathologic lesions and cellular tropism of natural infection of RVFV in young lambs as follows; (1) Enlarged and friable liver, the liver also becomes dark because of severe congestion, there is a proliferation of macrophages with predominant neutrophils microscopically (2) There is swollen gallbladder accompanied by hemorrhages, and there is intravascular cellular debris in small vessels and capillaries (3) Lymphadenopathy (4) Hemorrhages on the thymus and kidney (5) Pulmonary edema and congestion (6) Hydrothorax (7) Hemorrhages are seen on the epicardium and endocardium (8) Sometimes there are hemorrhages on the peritoneal surface and abomasal mucosa. (9) Hemorrhages are also seen on the skin and subcutis, and in the nervous system inflammation of the brain tissue is seen. RVFV can be differentiated from the following diseases: Bluetongue disease, Bovine ephemeral fever, Nairobi sheep disease, leptospirosis, brucellosis, Vibrios, Trichomoniasis, and other diseases associated with hemorrhagic fever, and abortion.

Past Studies

Rift Valley Fever virus (RVFV) was identified in Nigeria several years ago in a sheep brought from South Africa through international trade or the movement of animals (Ferguson, 1959). Nevertheless, some indigenous animals exhibit antibodies against the Rift Valley Fever virus. Four strains of the virus were also identified from sheep, mosquitoes, and culicoides (Lee, 1970). Evidence from previous studies shows that RVFV exists in Nigeria (Table 1) but it is difficult to detect or to confirm due to inadequate diagnostic tools and health facilities in both veterinary and human hospitals or it is misdiagnosed as malaria due to its febrile characteristics.

In 1980, a study was conducted by Oyewale Tomori, from the virus research laboratory, at University of Ibadan, Ibadan, Nigeria where he isolated RVFV from human blood from different parts of Nigeria particularly Enugu, Ibadan, Kainji, Jos, and Makurdi, and detected the presence of antibodies against the virus. Epidemiological data from hospitals were also used, and a sample from both adults and children was collected for the study.

In 1982, Ezeifeka *et al*., (1982) studied a total of 1106 serum samples collected from camels, cattle, goats, and sheep collected from Sokoto and Kaduna States in Nigeria. These sera were tested for the presence of antibodies against RVFV using the agar gel immunodiffusion method. He claimed that camels, cattle, goats, and sheep had 3.13%, 2.85%, 0.98%, and 6.67% antibodies against RVFV respectively.

Between 1985 and 1989, Olaleye et al. (1996) conducted a study on RVFV in animals and humans. For the animals, a total of 2,255 samples were collected from 6 domestic animals in Nigeria, 259 (11.5%) had haemagglutination-inhibiting and neutralizing antibodies (camels (3.3%), cattle (10.2%), horses (9.8%), goats (10.4%), and sheep (18.7%)) (Olaleye *et al*., 1996). Plateau state was discovered to have the highest prevalence of RVFV antibodies with 18.4%. Also, animals (with ≥ 3 years of age) had a higher prevalence of antibodies to RVFV. Furthermore, longitudinal studies showed seroconversion to RVFV in 10 out of 210 (4.8%) animals that were kept under observation. All the seroconversions noticed occurred in the wet season (Olaleye *et al*., 1996). For the humans, 3,121 human sera samples were collected from diverse population groups in 6 ecological zones in Nigeria (Olaleye *et al*., 1996). A total of 461 sera (accounting for 14.8%) demonstrated haemagglutination-inhibiting antibodies and 390 out of the 461 reactive sera (84.6%) showed neutralizing antibodies. Livestock farmers and wildlife wardens had significantly higher exposure to RVFV compared to other categories of people tested. Also, based on age, adults (≥ 30 years) had a higher rate of positive reactions than younger age groups.

In 2014, Bukbuk et al. (2014) sampled 297 sera from humans in Borno State, Nigeria. Using RVFV-IgG-ELISA, a total of 42 (14.1%) showed seropositivity in these individuals. RVFV was compared to viral hemorrhagic fevers (Lassa fever and Crimean-Congo Hemorrhagic fever) in Nigeria, and RVFV had the highest seroprevalence among others.

In 2017, there was an account of the RVFV outbreak in Sokoto, in an animal market in Illela bordering Niger where various animals including goats, sheep, cattle, and dromedary showed positive results following serological tests (Lagare *et al.,* 2019). Another outbreak also occurred in a village in Adamawa state bordering Cameroon where several cattle were affected. A subsequent outbreak occurred in Borno state and a village in Kano state. Rift Valley Fever virus might have been introduced into Nigeria because of the international movement of animals through land borders considering it a transboundary animal disease.

Table 1: Summary of past studies on RFV in Nigeria (1900 - 2017)

State studies	Year of studies	Targeted species
Enugu, Ibadan, Kainji, Jos, and Makurdi	1980	Humans
Sokoto and Kaduna	1982	Camels, cattle, goats, and sheep
Ibadan, Ile-Ife, Plateau, Maiduguri, Kano, Adamawa, Abuja, Jebba, Shao, Fasola, and Odeda	1985 and 1989	Humans and animals (sheep, goats, cattle, horses, and camels)
Borno	2014	Humans
Sokoto	2017	Goats, sheep, cattle, and dromedary

Present Studies

In 2018, Opaleye et al. (2108) sampled 265 workers in two livestock markets and farms for Rift valley fever virus (RVFV) in Ibadan, Nigeria. A total of 14 (5.3%) individuals tested positive for anti-RVFV IgG. It was noticed seropositive were more among livestock keepers (5.6%) compared to butchers (3.6%) (Opaleye *et al.*, 2108). Most of the workers that visited the northern part of the country's livestock-rearing areas had a higher rate of infection than those that did not visit.

In 2019, Oragwa *et al.* (2022) worked on the seroprevalence of RVFV in 196 people including livestock keepers (n = 20), abattoir/slaughterhouse workers (n = 55), and butchers (n = 121) in Borno, Benue, and Sokoto States in Nigeria. A total of 39 (19.9%) samples out of the 196 samples were positive for antibodies against RVFV, distributed as 21.5% (26/121) for butchers, 20% (4/20) for livestock keepers, and 16.4% (9/55) for abattoir workers. Based on states, 17.4% (8/46) of Benue, 21.7% (15/69) of Sokoto, and 19.8% (16/81) of Borno States samples were seropositive.

A cross-sectional study conducted in one forest reserve, Gidan waya Jema'a Local Government Area, Kaduna state in northwest of Nigeria, shows a hidden circulation of Rift Valley Fever virus among a group of sheep kept in that community using a serological test (Adamu *et al.*, 2020). However, factors that influence the occurrence of Rift Valley fever should be studied in the forest reserve as it may differ from other determinants in other regions, and the season or period of the year in Nigeria.

Rift Valley fever virus is also circulating among wild animals. Evidence from a seroprevalence study found that elephants, zebra, eland, wildebeest, waterbuck, and kudu that live in the Yankari game reserve in Bauchi state, Nigeria possess antibodies against RVFV (Atuman *et al.*, 2020). Moreover, findings by Joseph *et al.* (2020) revealed that high-level

antibodies against the Rift Valley fever virus exist among slaughtered ruminants in Jos, Nigeria.

A cross-sectional study was conducted using participatory epidemiology in Niger state in north central part of Nigeria in a community of nomadic pastoralists. The nomadic pastoralists describe RVF as one of the diseases affecting their cattle which they referred to it as "Gabi gabi", they also explained that the disease is associated with high fever, diarrhea, storm abortion, and neonatal death. Based on this survey, increased mosquitoes, high population of cattle, and stagnant water influence the occurrence of RVFV infection in their community, and following serological tests using ELISA, 11 out of 97 cattle that were sampled, were found to be seropositive in the herd (Alhaji *et al.*, 2020). In the same vein, age, breed, and sex are not a determinant in the occurrence of Rift Valley in Nigeria among cattle herds, because the different breeds of animals that vary in sex and age exhibit Rift Valley fever Immunoglobulin M prevalence of 5.6% (Alhaji *et al.*, 2020).

Future Studies

Looking at the past and present study of RVF in Nigeria, Rift Valley Fever is silently circulating among domestic and wild animals which may pose a great danger to the human population and harm the economy. Further studies of RVF should focus more on studying the possible reservoirs of RVF. Also, the usage of molecular techniques in characterizing RVFV is needed to assist with the development of a vaccine against this virus.

Conclusion

Based on past and present studies conducted, Rift Valley fever virus has been in circulation in Nigeria for so many years. There is little research conducted on the seroprevalence of Rift Valley fever in the southern part of Nigeria compared to the northern region. However, in the southern part of Nigeria, there is the presence of large water bodies such as rivers, oceans, and streams, greater annual rainfall throughout the year with a high density of animals due to their abundant grazing land and favorable climate. This shows that there may be higher antibodies against Rift Valley fever virus in animals living in the south than in the north when studied. Moreover, there is a massive movement of animals from north to south for grazing and trade.

Looking at the northern part of Nigeria, which shares borders with other African countries that have a record of Rift Valley fever virus outbreaks such as Cameroon and the Niger Republic and there is always international movement of animals through those borders. There are two main scenarios: either animals from the northern region are infected with the virus due to the transboundary movement of animals and later transmit

the virus to the animals in the southern region of Nigeria or there is natural infection.

Seroprevalence studies need to be conducted in all regions of the country for early detection of the disease. Considering the climatic factors that influence its occurrence, more research should be done in various regions of the country. Adequate diagnostic tools should be used when conducting further research on Rift Valley Fever virus to identify and characterized different strains of the virus. Surveillance should also be increased, a report from farmers and animal handlers should be obtained on any case having similar characteristics with Rift Valley fever. Movement of animals during grazing or around interstate borders should be monitored. Finally, antemortem and postmortem should be implemented in all abattoirs across Nigeria.

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