



International Journal of Current Research and Academic Review

ISSN: 2347-3215 (Online) Volume 13 Number 1 (January-2025)

Journal homepage: <http://www.ijcar.com>



doi: <https://doi.org/10.20546/ijcar.2025.1301.010>

Epidemiology and Public Health Significance of Rift Valley Fever: A Review

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Abstract

Mammals can contract Rift Valley Fever, an acute viral disease spread by vectors. Because of its ability to spread like wildfire and the absence of viable defenses, the virus is included as a priority pathogen on the World Health Organization's Blueprint list. A virus that is spread by mosquitoes that causes ruminant and human zoonosis has serious negative effects on public health and the economy when it breaks out in Africa and the Arabian Peninsula. A virus belonging to the family Bunyaviridae, which is a group of enclosed single-stranded RNA viruses, is the cause of the illness. It is classified as a phagovirus. Compared to adults, young animals have a far higher chance of being impacted. In mature sheep, cattle, and goats, abortion is a frequent result. Through interaction with diseased livestock and mosquito bites, humans can contract the disease. Large-scale morbidity and mortality in cattle and humans can result from outbreaks. A number of kinds of mosquitoes are the main vector for the spread of Rift Valley disease. Vertically infected eggs from the main *Aedes* species vectors, which emerge after heavy rains and widespread flooding, serve as a reservoir for the virus in between epidemics. Rift Valley Fever has no approved specific treatment; supportive care in general is the means of management. Based on epidemiological characteristics, Rift Valley Fever is diagnosed, and the organism's identification provides confirmation. Mosquito control can lessen the persistent method of preventing Rift Valley Animal vaccinations against fever are the best way to prevent fever infection in endemic areas. Effective vector management programs should also be put in place, and an ongoing human-animal surveillance system should be established and strengthened.

Article Info

Received: 22 November 2024

Accepted: 28 December 2024

Available Online: 20 January 2025

Keywords

Control and Prevention, Epidemiology, Mosquitoes, Public health, Rainfall, Rift Valley fever.

Introduction

Acute virus-borne disease of mammals, Rift Valley Fever is spread via vectors. The genus *Phlebovirus*, belonging to the family *Bunyaviridae*, is the cause of Rift Valley fever. Elevated death rates in lambs, youngsters, calves, and adult sheep are indicative of outbreak incidents. In mature sheep, cattle, and goats, abortion is a common consequence. In fatal cases and aborted fetuses, hepatitis with focal hepatic necrosis is a principal lesion (Mohamed *et al.*, 2010). RVFV is listed as one of the priority pathogens in WHO Blueprint list

due to its epidemic potential and lack of effective countermeasures (Golnar *et al.*, 2018). RVF is now considered a major challenge in global zoonotic disease control (Pepin *et al.*, 2010).

Rift Valley fever (RVF) is a fatal zoonotic disease of mainly human and ruminants caused by a member of *Phlebovirus* genus of the family *Bunyaviridae*. Since its first description in Kenya in 1931 (Metras *et al.*, 2016). RVF has been reported in Sub-Saharan Africa, as well as in Egypt (1977), in Madagascar (1979), in the Arabian Peninsula (2000), and in the Islands of the Comoros

archipelago (2007) (Metras *et al.*, 2016). Rift Valley fever outbreaks have been reported in Tanzania, South Africa, Mauritania, Senegal and Sudan. In 2001-2002 RVF outbreaks were reported beyond Africa in Saudi Arabia and Yemen (Mhina *et al.*, 2015), but has the recognized potential to spread globally (Weaver and Reisen, 2010).

Heavy rains and flooding are linked to outbreaks in Kenya, creating the perfect environment for mosquito vector proliferation and the subsequent onset of disease. As such, RVF epizootics are cyclic and periodic in nature, sometimes occurring as explosive outbreaks that cause significant morbidity and mortality in humans and animals (Abdala *et al.*, 2020). RVF is a primarily affecting domestic livestock (cattle, sheep and goats) (Metras *et al.*, 2016), and it is a zoonotic disease that not only affects cattle, camels, sheep and goats but also people and wildlife (Muga *et al.*, 2021).

Rift Valley fever virus is transmitted among ruminants by mosquito bites mainly belonging to the *Aedes* and *Culex* species and by direct contact with body fluids of viremic animals (Dohm *et al.*, 2000). When vertically infected adult *Aedes* spp. mosquitoes emerge from nesting sites and bite vulnerable livestock in Africa, the rainy season's related transmission of the virus commences. This, in turn, amplifies the virus and permits horizontal transmission through various biting vectors. Handling of such tissues by humans has been found to be significantly associated with infection (Anyangu *et al.*, 2010). Transmission is mostly horizontal, but a vertical mode was described for some *Aedes* species (Chevalier *et al.*, 2005). The virus that causes Rift Valley fever is conveyed in the eggs of *Aedes* mosquitoes, which develop in the wide grassland expanses in solitary depressions known as dambos. At flooding of the dambos during periods of extensive and widespread rainfall, the eggs of the *Aedes* mosquitoes hatch and the subsequent adults transmit the virus to domestic animals including sheep, goats, cattle, camels, and buffalos (Mondet *et al.*, 2005). Early detection and implementation of appropriate measures, which are essential to minimize the consequences of outbreaks, require a deep understanding of transmission, spread and persistence mechanisms (Chevalier, 2013).

Liver damage, weak-born offspring, abortion, and neonatal mortality are the hallmarks of the disease in camels and ruminants. Human infections typically present as minor illnesses similar to the flu or with no symptoms at all. In severe disease, it causes hemorrhage,

encephalitis, visual disturbances and death (Ibrahim *et al.*, 2021). Because of its potential to cause severe disease in both animals and man during outbreaks, RVFV is considered a major zoonotic threat which is classified as a category A overlap select agent by the Centre for Disease Control (CDC) and as a high-consequence pathogen with potential for International spread (List A) by OIE (Kasye *et al.*, 2016; Ibrahim *et al.*, 2021).

Furthermore, RVFV is also considered as a potential bioterrorism tool that could have direct (morbidity and death) and indirect (restriction in international trade) impact in countries that are free from the virus (Sindato *et al.*, 2011). Rift Valley fever has a direct impact on livestock and human health as well as on trade (Weaver and Reisen, 2010). There is no specific treatment for RVF. However, two vaccines are available and are commonly used for control of RVF in endemic countries: a live attenuated vaccine and a formalin inactivated vaccine (Kasye *et al.*, 2016). There are various approaches for control, including controlling the animal trade, educating exposed human populations, and carrying out larvicides in vector breeding places and/or insecticide spraying. However, the disease is usually well established in animal populations by the time when the first human cases are observed (Chevalier, 2013).

One of the busiest livestock trading hubs in the Horn of Africa is the Somali region of Ethiopia. According to different estimates, this region accounts for 60-80% of Somalia's cattle exports, with the majority of the trade being informal across borders. Rift Valley fever was reported to OIE following positive serological tests but no clinical disease (Samrawit, 2018; Sindato *et al.*, 2011).

The geographical localization of the country, associated with large commercial ruminant trade and pastoralist's movement makes Ethiopia at risk for RVF occurrence (Samrawit, 2018). Ethiopia has been subject to three bans in total since 1997-1998 due to pandemic disease situations in Kenya and Somalia.

Its geographical proximity to RVF endemic countries like Kenya, Sudan and Somalia, the nature of livestock movements across the international border and the ease with which infected mosquitoes can be moved longer distances by the help of wind can lead to the conclusion that Ethiopia will always be vulnerable to clinical RVF during the epizootic periods of the disease in East Africa (Kasye *et al.*, 2016).

Therefore the objectives of this paper are; to review the epidemiology and public health importance of Rift Valley Fever and to provide, afford facts and aware about rift valley fever on way of prevention and control

General Justification about Rift Valley fever

Etiological agent and Taxonomy

Rift Valley Fever caused by the virus a member of the genus *Phlebovirus* in the family *Bunyaviridae* (Parker and Parker, 2002). The RVFV genome is organized in three negative-sense, single-stranded RNA segments termed large, medium, and small, with a total genome length of 11.9 kb (Samy *et al.*, 2017). Rift Valley fever Virus is an enveloped virus with a diameter of 90 to 110 nm and a core element of 80 to 85 nm (Angelle, 2009). Transcription and replication take place in the cytoplasm. The genome segments of bunyaviruses encode four structural proteins: the viral polymerase on the large segment, two glycoproteins (Gn and Gc) on the medium segment, and the viral nucleocapsid protein on the smallest segment (Bouloy and Weber, 2010).

History of Rift Valley Fever

About 1915, the disease was first discovered in sheep in Kenya, but the virus wasn't isolated until 1931. RVF virus has caused serious epidemics among sheep and cattle in the east and West Africa, led to death of great numbers of lambs, in 1931 during an outbreak investigation of a sheep epizootic on a farm in the Great Rift Valley of Kenya (Angelle, 2009). While RVF was originally associated with livestock mortality, recent outbreaks have resulted in increased fatality rates in humans (Adam *et al.*, 2010). Recent East African outbreaks in Tanzania, Kenya, and Somalia caused 478 human deaths in 1998 and 309 in 2007. During the 2007 outbreak in Sudan, 698 cases and 222 deaths were recorded. Recent RVF outbreaks have been characterized by severe infection and death in humans, with a high case-fatality rate of 50% for the hemorrhagic syndrome form (Yousif, 2016).

Insect Vectors

The primary vector for RVF transmission are mosquitoes. The female mosquito is the only one that consumes blood because she requires the protein to lay eggs. The water's edge is where mosquitoes will lay their eggs. The eggs of the mosquito will hatch into larvae, sometimes called wigglers, and then into pupae,

sometimes called tumblers. For survival, the pupae and larvae must reside in water. The pupae will change into adult mosquitoes (FAO, 2005). Mosquitoes, mainly those of the *Aedes* and *Culex* genera, are both reservoirs and vectors for RVFV, making them able to maintain RVFV and transmit it transovarially to their offspring (through eggs) (Himeidan *et al.*, 2014; Mansfield *et al.*, 2015) *Aedes* and *Culex* mosquito species are vectors of this virus, which affects not only sheep, goats, buffalo, cattle, and camels but also human beings (Clark *et al.*, 2018; Abdallah *et al.*, 2015).

Epidemiology of RVF

Distribution and Source of infection

Distribution: Rift Valley fever Virus caused a large epizootic in 1950–1951 in South Africa when an estimated 100,000 sheep died and 500,000 aborted (Linthicum *et al.*, 2016). It has great potential for spread to other countries. A Rift Valley fever-like disease is reported in sheep in India (Radostits *et al.*, 2006). Earlier in 2019, Kenya reported RVF in cattle and sheep (OIE, 2019). Many countries in Eastern Africa's tropical and southern regions are endemic to the disease. Eastern and Central Africa was where the disease epizootics were most common. The first thoroughly investigated epizootic begins in 1930 (Bird *et al.*, 2009).

Source of infection: Since they are the primary amplifying hosts, ruminants are particularly vulnerable. When an animal is afflicted, they experience a noticeable but brief viremia, which helps the disease spread by biting insects. Moreover, milk and excrement contain the virus. Trade animals are suspect as the source of infection to previously free areas (Radostits *et al.*, 2006). During viremia period, blood, tissue of affected animals, aborted fetus and fomites are source of infection (Samrawit, 2018).

Host Range and Susceptibility

The potential globalization of RVFV is facilitated by the presence of susceptible domestic animal hosts and mosquitoes in many parts of the world (Linthicum *et al.*, 2016). Rift Valley fever virus primarily affects livestock and can cause disease in a large number of domestic animals (this situation is referred to as an "epizootic") (Samrawit, 2018).

Host susceptibility depends on age and animal species (Sindato *et al.*, 2011). Many animal species are affected by mild to severe sickness caused by Rift Valley fever;

the younger the animal, the higher the chance that the infection would be fatal; morbidity and death are inversely correlated with animal age. Disease severity is also dependent on the species of the animal, and may be specifically virulent in sheep, followed by other commonly domesticated animals (Grossi-Soyster and Labeaud, 2020). The disease affects cattle, sheep, goats and camels with mortality rate reaching 30% and 100% in adult and young animals, respectively (Mhina *et al.*, 2015). Pigs, rabbits, guinea pigs, and poultry are not susceptible to infection, but camels, domestic buffalo, primates, humans, mice, rats, ferrets, and hamsters are, and goats somewhat so. A large number of different African wildlife species also have seropositivity in endemic areas (Radostits *et al.*, 2006). Amphibians and reptiles are resistant to RVF virus (Samrawit, 2018).

Risk factors and Incidence

Since The disease Rift Valley fever is an emerging zoonotic vectorborne disease representing a threat to animal and human health, and livestock production (Eisa *et al.*, 1977). Age of the animal is an important risk factor for severe disease: young sheep are particularly susceptible to RVF related illness mortality among lambs is 90% as compared to 10% among adult sheep (Angelle, 2009). Factors influencing the environment; the size of the vector population affects the disease's occurrence. As a result of the vector population's ability to spread out from permanent water sites and breed in surface waters in typically arid regions, it is most prevalent during periods of intense rainfall. Risk factors for animals: miscarriages and occasional deaths in adult sheep and cattle are possible, but losses are mostly caused by mortality in young lambs and calves. Lambs are more likely than calves to die. Indigenous breeds may have in apparent infections (Radostits *et al.*, 2006).

The prior outbreaks of RVF in Tanzania were caused by a number of epidemiological reasons. Farming practices, weather conditions (strong rains akin to an El Nino), vector activity, the existence of a sizable population of ruminant species, and meat-eating customs were among them. Compromised animal products, such as meat and milk, were another source of potential exposure. RVF spread in pastoral communities was mostly caused by consumption patterns, which were significant epidemiological determinants. Another factor for RVF occurrence and spread was animal movement (Sindato *et al.*, 2011). Aerosolization is generally a risk observed in occupational settings, such as slaughterhouses, where animal bodily fluids may be aerosolized during

processing and handling (Grossi-Soyster and Labeaud, 2020).

Morbidity mortality and outbreaks

For humans, the case fatality rate is usually less than one percent, whereas adult cattle, goats, buffaloes, and people are regarded as somewhat susceptible and have mortality rates normally less than ten percent. Equines, pigs, dogs and cats are categorized as resistant and infection is unapparent. It can result in significant infant mortality and abortion in pregnant animals. In humans, RVF results in a severe sickness akin to influenza, occasionally leading to further hemorrhagic complications and even death. It generates significant epidemics across its area at unpredictable 5-35-year periods (FAO, 2000). With a 70%–100% death rate, young animals including lambs, youngsters, puppies, and kittens are thought to be particularly vulnerable. Sheep and calves are considered as highly susceptible with mortality rates between 20%-70% (Bird *et al.*, 2009; Pepin *et al.*, 2010).

Outbreaks related RVF

Thus, unique geographical and temporal patterns that are closely linked to particular environmental factors connected to mosquito vectors characterize RVFV outbreaks in Africa. These vectors, in turn, influence the maintenance (enzootic) and transmission (epizootic) cycles of the virus (Logan, *et al.*, 1991; LaBeaud *et al.*, 2015). The first outbreaks outside Africa occurred in 2000, in Saudi Arabia and Yemen (Samy *et al.*, 2017). Resulting in 883 human cases with 124 deaths case-fatality rate of 14% in that country and 1,328 human cases and 166 deaths in neighboring Northwestern Yemen (Yousif, 2016).

Rift Valley fever Virus has not apparently become endemic outside Africa, but seropositive animals have been detected in Saudi Arabia (Samy *et al.*, 2017). The occurrence of RVF epidemics is associated with climatic changes with increased rainfall resulting in widespread flooding and resultant swarms of mosquitoes (Sindato *et al.*, 2011). The epidemic component of the maintenance cycle occurs infrequently and involves exceptionally heavy rainfall over an extended period up to many months, resulting in epizootics and epidemics that occur approximately every 5 to 15 years (Linthicum *et al.*, 2016). After periods of heavy rainfall and flooding, more RVFV-infected mosquitoes are proposed to hatch, thereby passing the virus to humans and animals to

produce a disease outbreak (Meegan *et al.*, 1978; Mamy *et al.*, 2011).

Opportunities for predicting rift valley fever outbreaks

Prediction of RVF can be improved by having a good national system, considering and following alert messages from international organizations and strengthening use of climate data (Sindato *et al.*, 2011). RVF epidemics are strongly correlated with periods of higher-than-average rainfall in Yemen, Saudi Arabia, and Africa. Furthermore, there is a strong correlation between the high rainfall that happens during the warm phase of El Nino and RVF outbreaks in East Africa (Jebara, 2007).

Routine surveillance for RVFV in African countries is limited and outbreaks are underreported. Proxy measures such as the normalized difference vegetation index (NDVI), monitoring of the El- Nino Southern Oscillation (ENSO) events and the sea surface temperature anomalies between Indian and Atlantic oceans have been used to predict when and where RVF outbreaks may occur (Clark *et al.*, 2018).

Rainfall amounts influence the amount of vegetation, which increases above average and may be tracked via satellite photos (See Figure 2). This situational monitoring can assist in creating risk maps for potential RVF outbreaks. These discoveries have made it possible to use satellite imagery and weather/climate forecasting data to create forecasting models and early warning systems for RVF. Early warning systems, such as these, could be used to detect animal cases at an early stage of an outbreak, enabling authorities to implement measures to avert impending epidemics (Jebara, 2007).

Figure 1 and 2 show clearly that Eastern Africa was at risk to RVF in January 2007. The dark zones represent regions that have more than normal vegetation coverage during the same period and are zones at risk for vectors proliferation and for the occurrence of RVF outbreaks in animals and in humans (Jebara, 2007).

Mode of Transmission cycles and vector ecology

To animals, RVFV is mainly transmitted by a range of mosquito species (*Aedes*, *Anopheles*, *Culex*, *Eretmapoites*, *Mansonia*), but has also been shown to be transmitted by other vectors e.g. sandflies (Bouloy and Weber, 2010). Mosquito vectors in the genus *Aedes* are

responsible for RVFV maintenance (primary vectors), while those in the *Culex*, *Mansonia*, and *Anopheles* genera are responsible for RVFV amplification (secondary vectors) in natural environments (Campbell *et al.*, 2019). *Aedes* spp. are the most important mosquitoes involved in vertical transmission of RVFV, and *Culex* and *Mansonia* spp. are the most important horizontal vectors of the virus (Linthicum *et al.*, 2016).

The most frequent link between Rift Valley fever and mosquito-borne outbreaks during years of high rainfall is established. An RVF epizootic is typically reported in years with high rainfall and/or localized flooding. Excessive rainfall facilitates the hatching of mosquito eggs, often belonging to the *Aedes* genus. The RVF virus infects the mosquito eggs naturally, and the resulting mosquitoes then spread the virus to the livestock they feed (Parker and Parker, 2002). Mosquitoes can transmit diseases to animals during the viremic phase. Viremia can last for six to eight days or for six to eight hours. There is no carrier state in animals (FAO, 2018; Linthicum *et al.*, 2016).

Long-distance transmission of a large number of infected mosquitoes by wind or air currents is possible. This could cause the virus to spread quickly across national borders or even between regions. This could have had a role in the spread in 1977 and 1993 both to and within Egypt. Long-distance transportation of smaller numbers of infected mosquitoes is also possible using cars and airplanes. While humans can become infected from mosquito bites, the majority of human cases are thought to result from handling the blood, tissues, secretions or excretions of infected animals, notably after abortion (FAO, 2018).

Although biting midges, black flies, and ticks have also been found to harbor the virus, this does not prove that they are capable biological vectors. The virus's main amplifying hosts are sheep and cattle. The virus that causes Rift Valley fever can spread vertically between mosquito generations without going through a cycle of vertebrate hosts. Additional risks of transmission include mechanical transmission, laboratory aerosol exposure, fomites, and ingestion of animal products (raw meat and unpasteurized milk). An enzootic cycle including *Aedes* mosquitoes, which can pass the virus vertically to their progeny, can sustain the infection. Epizootic outbreaks are often linked with unusual rains or warm seasons, favoring the hatching of infected *Aedes* eggs that are then able to initiate the virus circulation (USAHA, 2008).

Public Health and Socio-Economic Importance

Public Health Significance

When humans handle sick animals, help with animal birth, or slaughter livestock, they may come into touch with the blood or bodily fluids of an infected animal and contract RVFV. Raw milk or meat consumption is potential sources of RVFV, although transmission via these routes has not been confirmed (Nyakarahuka *et al.*, 2018). These routes beside direct contact with infected animal tissues include inhalation of aerosolized infected fluids during slaughtering of infected animals or during the birthing process, orally, laboratory infection (frequent) and transmission through bites of infected mosquito vectors (Archer *et al.*, 2013). Though infrequent, vertical transmission also occurs among both humans and animals. In rare cases, *Anopheles*, *Aedes*, and *Culex* mosquitoes can transmit the virus to humans. *Aedes* mosquitoes are considered to be the major maintenance host and source of RVFV outbreaks (Yousif, 2016), although currently there is no evidence for person-to-person transmission of RVFV (Shabani *et al.*, 2015).

The majority of RVF patients either show no symptoms at all or have a moderate disease with fever and liver abnormalities. Inflammation of the retina, which is a structure that connects the nerves in the eye to the brain, is the most frequent side effect of RVF. Consequently, between 1% and 10% of afflicted individuals may experience some degree of irreversible visual loss (Parker and Parker, 2002). The sickness usually goes away on its own in four to seven days in simple cases. Most instances are not severe (FAO, 2018). Humans with Rift Valley fever typically recover spontaneously from a moderate, acute febrile illness. In small proportion of cases the disease in human it can be associated with severe jaundice, rhinitis, encephalitis and haemorrhagic manifestations and death (Mhina *et al.*, 2015). Rift Valley fever can also cause human abortions, still births, and congenital infections (Grossi-Soyster and Labeaud, 2020).

Because of the zoonotic nature of the virus, specific occupational groups are at increased risk of infection (Archer *et al.*, 2013), such as animal herdsman, abattoir workers, and other individuals who work with animals in RVF-endemic areas (areas where the virus is present). Those who engage in high-risk occupations, such as veterinary care and slaughterhouse operations, are more likely to get the virus from an infected animal.

International travelers increase their chances of getting the disease when they visit RVF-endemic locations during periods when sporadic cases or epidemics are occurring (Parker and Parker, 2002). Rift Valley fever Virus is considered a Category A pathogen in the Center for Disease Control and Prevention (CDC)'s Bioterrorism Agent/Disease classifications, and as an overlap select agent by the Health and Human Services and United States Department of Agriculture (USDA) Federal Select Agents Program (Grossi-Soyster and Labeaud, 2020). Rift Valley fever Virus is adaptable to weaponization, as shown by past studies of the United States biological warfare program (Angelle, 2009).

Due to the lack of specific treatment available for RVF, the management of suspected cases is usually based on supportive therapy (Petrova *et al.*, 2020). Because the virus is a biosafety level three pathogen, handling it in a lab setting with tight biosafety cabinet guidelines is necessary to avoid human exposure. As RVF is a zoonotic disease, all precautions should be taken to protect the health of the persons engaged in livestock industry (Kasye *et al.*, 2016).

Due to the lack of a licensed vaccine, prevention strategies for RVFV infection are limited to the use of personal protective equipment to prevent nosocomial infections as well as standard measures to prevent exposure to mosquito vectors (bed nets, long clothes) (Petrova *et al.*, 2020). Avoiding exposure to blood or tissues of animals that may potentially be infected is an important protective measure for persons working with animals in RVF-endemic areas (Parker and Parker, 2002).

Socio-Economic Importance

Rift Valley fever can have catastrophic economic impact on meat and dairy producers. Rift Valley fever virus is a high priority pathogen because of its potential for severe economic harm to livestock (Angelle, 2009). The first reported direct socio-economic impact of RVF was on livestock producers due to high levels of mortality and morbidity in animals (Samrawit, 2018). This represents an important loss of stock, especially in young ruminants (Kasye *et al.*, 2016).

The disruption of livelihoods, markets, and the meat business resulting from a prohibition on cattle slaughter, coupled with the sickness and mortality of livestock, had significant social repercussions. RVF was considered by the communities to be a serious disease than HIV/AIDS

due to the fact that the RVF outbreak had made them poor as they could not sell their animals, and they went hungry as they could not drink milk and eat meat (Sindato *et al.*, 2011). It has been noted that livestock producers are negatively affected by measures that ban exports or slaughter and remove or reduce opportunities for earning income (Muga *et al.*, 2015).

Pathogenesis

Age affects how an infection progresses and turns out in lambs and calves, as hepatocytes are the main site of viral replication in these animals. In very young animals, hepatic lesions progress from degeneration and necrosis of individual hepatocytes to extensive necrosis throughout the liver resulting in hepatic insufficiency and failure (Radostits *et al.*, 2006).

When the Rift Valley Fever virus enters target tissues through a mosquito bite, a percutaneous injury, or aerosols entering the oropharynx, it multiplies quickly and to a very high titer. Critical organs like the spleen, liver, and brain are affected by the virus's pathogenic effects or immunopathological pathways after infection; in the absence of these, recovery is mediated by both nonspecific and specialized host responses. The virus is conveyed from the inoculation site by lymphatic drainages to regulate lymph nodes where there is replication and spin over into the circulation which leads to viremia and systemic infections (Samrawit, 2018; Radostits *et al.*, 2006).

Clinical Signs

Depending on the animal's age and the species it affects, the disease might present with different clinical signs. Animals that are younger have a far higher mortality rate than older ones. While mature cattle and camels are typically asymptomatic, sheep and goats are extremely susceptible. The animals typically display fever, lassitude, lesions in the spleen and liver, bloody diarrhea, and miscarriages. Severe disease can occur suddenly causing death without previous symptoms (Wright *et al.*, 2019). The most severe impact is observed in pregnant livestock infected with RVF, which results in abortion of virtually 100% of fetuses (Parker and Parker, 2002).

High numbers of simultaneous, spontaneous abortions among ruminants (so-called "abortion storms") and high mortality rates among young animals accompany epizootics (Campbell *et al.*, 2019). Spontaneous abortion

in pregnant animals also reduces future product generation capacity with the loss of offspring, influencing further financial burden (Grossi-Soyster and Labeaud, 2020). Infected animals develop necrotic hepatitis and hemorrhage (Bouloy and Weber, 2010).

One to six days can pass during the incubation phase. Newborn lambs incubate for 12-72 hours, mature sheep, goats, and cattle for 24-72 hours, and humans for 3-6 days. Rift Valley fever is characterized by high abortion rates and high mortality in neonates usually occurring after periods of heavy rainfall and clinical signs (Kasye *et al.*, 2016). Outbreaks are characterized by high levels of mortality in lambs, kids, calves and adult sheep. Abortion is a common outcome in adult sheep, cattle and goats. The morbidity rate in infected flocks is close to 100 percent (FAO, 2018).

Diagnosis

RVF is diagnosed by serological means (ELISA) using rain bands that are abnormally heavy, clinical symptoms and signs, storm abortions occurring in small ruminants, and other epidemiological considerations. When the organism is identified using RT-PCR techniques, the diagnosis is deemed confirmed. Because propagation of the virus requires strict laboratory guidelines (biosafety level 3 or 4) (Sindato *et al.*, 2011). Isolation of infected virus from appropriate specimen and its identification can establish diagnosis. Isolation of infecting virus in cell culture is most sensitive method of diagnosing viral disease (Kasye *et al.*, 2016).

Rift Valley fever outbreaks always represent a great challenge for human and animal diagnostic laboratories, as has been recently recognized in the first outbreak in Niger (Lagareet *et al.*, 2016). Due to the high containment level (biosafety level 3 (BSL3) required for handling of suspected RVF cases, diagnostic testing of RVFV is typically performed only in dedicated reference laboratories with trained biomedical staff. A conclusive diagnosis of RVFV infection necessitates, per WHO guidelines, the following tests: (1) real-time polymerase chain reaction (RT-PCR) detection of virus RNA in blood or plasma; (2) detection of anti-RVFV IgM and IgG antibodies; (3) detection of RVFV virus antigen and/or (4) RVFV isolation. The selection of an optimal assay depends on the timing of sampling relative to disease progression and the ability to detect antigenic (isolated virus, viral RNA) or immunological markers (IgM and IgG) (Petrova *et al.*, 2020).

Table.1 Countries where and years when RVF outbreaks were officially notified either to the OIE and ADNS for animals or to WHO for humans, since 2010 (Nielsen et al., 2020).

Country	Years of Notification	
	Outbreaks in Animals (OIE and ADNS)	Outbreaks in humans(WHO)
Botswana	2010/2014/2017	
Central African Republic		2019
Chad	2018	
Comoros	2010/2011	
Democratic Republic of Congo	2012	
Gambia		2018
Kenya	2018/2019	2014/2015/2018
Mali	2016/2017	
Mauritania	2010/2011/2012/2013/2014/2015	2010/2012
Mayotte (France)	2018/2019	2019
Mozambique	2013/2014/2016/2018	
Namibia	2010/2011/2012	
Niger	2016	2016
Nigeria	2017	
Rwanda	2012/2013/2014/2016/2017/2018	
Saudi Arabia	2010	
Sudan	2019	2019
South Sudan	2017/2018	
Senegal	2013/2014/2015/2016/2018	
Uganda	2016/2017/2018	2019
South Africa	2010/2011/2018	2010

Figure.1 Normalized Difference Vegetation IndexAnomaly Map (Jebara, 2007).

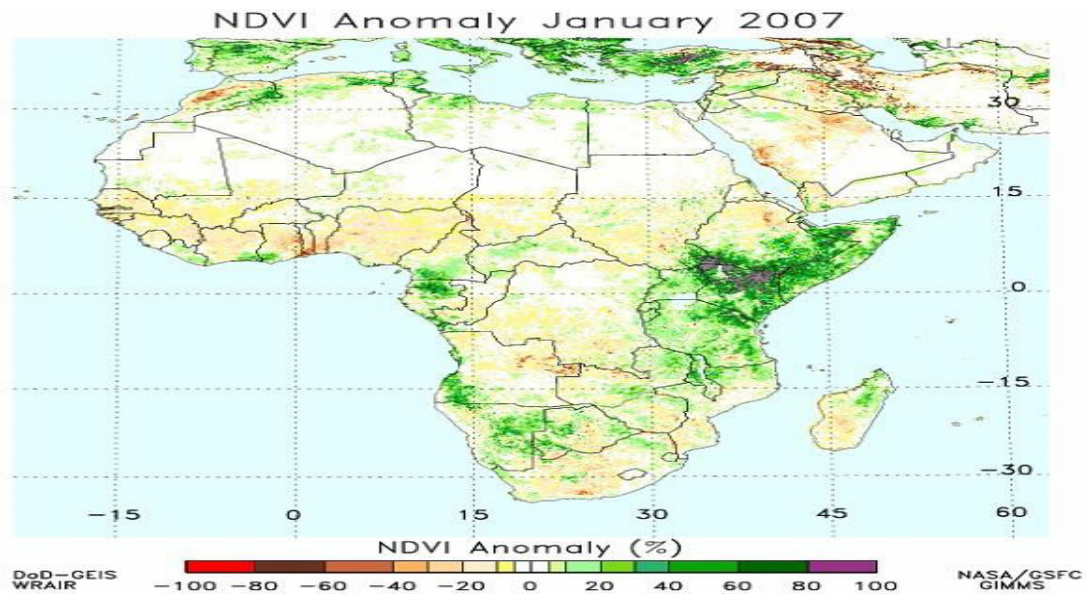
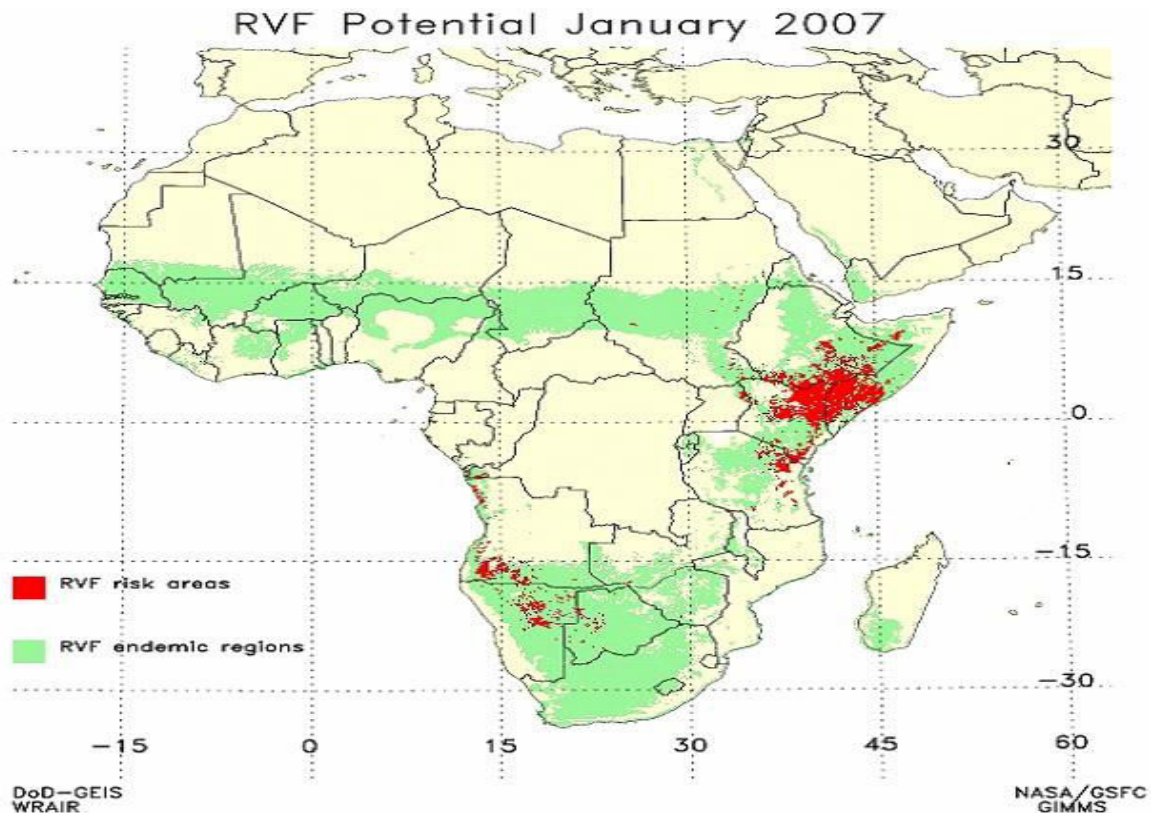


Figure.2 Risk Map for Rift Valley Fever for the Month of January 2007 (Jebara, 2007).



Treatment

There is no specific treatment for RVFV infection in humans or animals, but supportive care may prevent complications and decrease mortality (Nyakarahuka *et al.*, 2018). The severity of RVFV zoonosis, its capability to cause major epidemics among livestock and humans, and the lack of efficient prophylactic and therapeutic measures make infection with this pathogen a serious public health concern not only in endemic, developing countries, but also in many non-endemic industrial countries (Bouloy and Weber, 2010).

Prevention and Control

Priority should be given to preventative efforts as the first lines of defense against this disease, given the potential for increased hazards under continued climate change, increased worldwide travel, and expanding regional and international trade. Global efforts should focus on early detection and containment of RVF at its source in order to stop the disease's spread and eventually eradicate it. Safe discarding of infected animals and minimizing unsafe human-animal contact in the early stages of an outbreak (Yousif, 2016).

Nations that are vulnerable should take all necessary precautions to stop the disease from entering or spreading. When importing animals from locations known to be epizootic, it is important to closely monitor animal movement.

When infected mosquitoes begin to emerge, an RVF outbreak has begun. In theory, the control of mosquitoes can reduce the amplification and contribute to the mitigation or prevention of outbreaks (FAO, 2018).

Several control measures are described usually including the following: (i) control of livestock movements with respect to trade and export; (ii) vector control with an emphasis on larvicides in vector breeding sites rather than aerial sprayings targeting adults or (iii) vaccination of livestock if applicable (Nicolas *et al.*, 2013).

Individual protective measures for humans are challenging but attainable; however, it is extremely difficult to keep mosquitoes from livestock and impossible to prevent mosquitoes from contacting wild ungulate reservoir and amplifying hosts (Linthicum *et al.*, 2016).

The selection and application of pesticides has to adhere to both domestic and global guidelines, taking into account the impact on the environment. Currently, using pesticides that linger in the environment is prohibited. Applying insecticidal or repellent products topically to animals lowers the risk of infection in humans as well. Insect-proof housing could be considered as a way of protecting high-value livestock (FAO, 2018).

Besides the financial cost, ecological and health issues associated with the extensive use of insecticides should be considered. Precautions during animal exams, handling animals for milking or other care and maintenance behaviors, and slaughtering or breaking down carcasses should be observed to avoid contact with fluids and blood (Grossi-Soyster and Labeaud, 2020). Work with the virus and suspect materials should be conducted only with recommended personal protective equipment and biocontainment consistent with biosecurity level 3 (BSL 3) (FAO, 2018).

In Africa, a live attenuated vaccine based on the Smithburn strain is available and provides lasting protective immunity, but it is abort-genic in pregnant livestock (Botros *et al.*, 2006). Vaccinating animals is the most effective long-term strategy to prevent RVF infection in endemic locations. The Smithburn vaccine is a veterinary vaccination that is frequently administered in Africa. This vaccine was created and gives vaccinated animals lifetime immunity. This vaccine's drawback is that it induces teratogenesis and miscarriages in goats, cows, and ewes. Protective gears such as gloves and other appropriate protective clothing should be worn and care taken when handling sick animals or their tissues or any other suspected biological materials (Sindato *et al.*, 2011).

In North America or Europe, no RVFV vaccination is currently authorized for use in humans or animals. Animal studies have shown that certain vaccinations, both inactivated and live-attenuated, are effective. Owing to vaccine safety concerns, developing human RVFV vaccinations has been difficult. An experimental human vaccine, TSI-GSD200, has shown some utility in laboratory workers, but has not been used extensively in other settings (Nyakarahuka *et al.*, 2018).

Conclusion and Recommendations

The RVF virus is the zoonotic virus that causes Rift Valley fever, which is spread by mosquitoes. Many animal species, including humans, are afflicted by the

illness. Epidemiologically, mosquitoes and susceptible domestic animal hosts are present in many places of the world, which facilitates the spread of Rift Valley Fever. It poses a threat to cattle output, results in serious human illness and mortality, and generates large financial costs in terms of public health. The confirmation of the organism's identity and epidemiological parameters form the basis of the RVF determination. The primary methods for lowering the prevalence of RVF are vector controls. There is no known cure for this condition, which is thought to be an occupational illness that affects veterinarians, dairy farmers, workers in abattoirs, and anyone who manage livestock.

The aforementioned conclusions lead to the following recommendations:-

- ✓ An efficient and appropriate vector control program should be implemented based on entomological surveys.
- ✓ An active and continuing human-animal surveillance system should be established and strengthened through collaboration between human and animal health authorities.
- ✓ It is necessary to provide vaccines that are safe, efficient, and reasonably priced to prevent infections in both humans and animals.
- ✓ Restrictions must be placed on the transfer of animals from overseas or from areas that were previously RVF-free.

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How to cite this article:

Begidu Tesfaye Mune and Tariku Geinoro Alleyo. 2025. Epidemiology and Public Health Significance of Rift Valley Fever: A Review. *Int.J.Curr.Res.Aca.Rev.* 13(01), 81-93. doi: <https://doi.org/10.20546/ijcrar.2025.1301.010>