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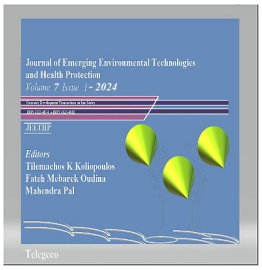

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Rift Valley fever: An emerging and re-emerging viral zoonosis of public health importance

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Abstract

Emerging and re-emerging viral zoonoses are an important cause of morbidity as well as mortality in developed and developing nations of the world. Rift Valley fever is a viral metazoonosis affecting both animal and human populations primarily in African nations. The epidemic of disease has a serious impact on human health. Rift valley fever is fatal in young animals. This review explores the virus's etiology, transmission dynamics, clinical manifestations in animals and humans, pathogenesis, economic implications, and preventive measures. Rift Valley fever virus transmission is primarily mosquito-borne, facilitated by climatic factors like heavy rainfall as well as flooding. Humans can also acquire the infection by direct contact with blood, tissues and body fluids from the sick animals. The disease causes severe economic losses through livestock mortality and trade restrictions, while human infections range from mild flu-like symptoms to severe neurological and hemorrhagic complications. The laboratory help is essential to make a confirmatory diagnosis of disease. Currently, no antiviral drugs are available for the treatment of disease. Prevention strategies include vaccination of livestock, vector control, and public awareness campaigns. By addressing these aspects, this review aims to guide effective public health interventions and mitigate the impact of Rift Valley fever virus outbreaks.

Keywords: Emerging zoonosis, Metazoonosis, Mosquito, Public health, Rift Valley fever, Vector control

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1. INTRODUCTION

Metazoonosis is a zoonotic disease that is transmitted biologically by invertebrate vectors, such as ticks, mosquitos, mites, rat flea, and tsetse fly (Pal,2007). There are many metazoonoses caused by diverse etiological agents that include viruses, bacteria, reckettsia, and protozoa (Pal,2007). Rift Valley fever (RVF) is an important emerging and re-emerging mosquito-borne viral zoonosis affecting domesticated ruminants, and also humans and is caused by Rift Valley fever virus that belonged to the Genus *Phlebovirus* and the Family *Phenuiviridae* family (Wright *et al*., 2019). The disease was first identified in 1931 during a major outbreak of abortion and necrotic hepatitis in Kenyan sheep (Nanyingi *et al*., 2015), Rift Valley fever has since spread across South and East Africa (Pepin *et al*., 2010). The region has experienced notable outbreaks, particularly in 1997–1998 and 2006–2007, both associated with heavy rains and flooding. The recurrent nature of these outbreaks underscores the importance of understanding the interplay between climatic factors and disease dynamics to mitigate future economic and health impacts. These environmental conditions not only facilitated the disease's spread but also led to significant financial losses for livestock owners (Pienaar and Peter, 2013). Rift Valley fever virus (RVFV) is endemic across most African countries (Musa *et al*., 2022), with outbreaks predominantly occurring during years of heavy rainfall, which facilitate mosquito-borne epidemics (Pepin *et al*., 2010). This virus significantly impacts domestic ruminants, including sheep, goats, cattle, and camels, causing high abortion rates and sudden deaths among young animals. In addition to affecting livestock, RVFV can infect humans and wild wildlife, generally causing mild illness in these populations (Connors and Hartman, 2022). The primary vectors for RVFV transmission are mosquitoes, particularly those from the *Aedes* and *Culex* genera, which play a crucial role in the spread of this disease (Nielsen *et al*., 2020).

Rift Valley fever virus exhibits resilience by surviving in the dried eggs of *Aedes* mosquitoes, with outbreaks triggered by the hatching of these eggs during heavy rainfall and localized flooding (Eastwood *et al*., 2020). Sheep and cattle are the primary amplifying hosts (Mansfield *et al*., 2015), but once the virus is amplified, it can be transmitted by various vectors, including multiple mosquito species and potentially other biting insects like ticks and midges. Additionally, animal products such as fresh, chilled, and frozen meat, wool, bones, skins, hides, and milk from

infected animals are considered potential sources of RVFV (Kwaśnik *et al*., 2021).

Rift Valley fever exacts a profound economic toll, devastating agricultural communities upon introduction with significant mortality rates among both livestock and humans. The disease inflicts nearly 100% mortality among young animals and induces high abortion rates in livestock (Lubisi *et al*., 2023). Beyond its direct health impacts, RVF imposes substantial economic burdens through disease management costs, including quarantine measures, restrictions on livestock movement, surveillance expenses, and intervention strategies. Moreover, public perceptions of risk can lead to a collapse in demand for affected products (Mariner *et al*., 2022). The objectives of this paper are to comprehensively review the evolving public health significance of Rift Valley fever virus. This includes analyzing its impact on both animal and human populations, assessing current epidemiological trends, exploring transmission dynamics, evaluating existing prevention and control measures, and identifying gaps in knowledge to guide future research and public health interventions effectively.

2. LITERATURE REVIEW

2.1. Etiology of Rift Valley Fever

Rift Valley Fever virus is a spherical enveloped RNA virus belonging to the *Phenuiviridae* family (formerly *Bunyaviridae)* within the genus *Phlebovirus*. It is responsible for causing Rift Valley fever (Wright *et al*., 2019). The virus possesses a genome composed of three segments: the short (S), medium (M), and large (L) segments, collectively forming a tripartite RNA genome (Mansfield *et al*., 2015). The L segment encodes the viral RNA-dependent RNA polymerase. The M segment not only codes for non-structural proteins (NSm) but also includes the genes for two envelope glycoproteins, Gn and Gc. The S segment encodes the nucleoproteins (N) and the second non-structural protein (NSm). These genomic components play essential roles in the virus's replication, pathogenesis, and interactions with host cells, contributing to the complexity and virulence of Rift Valley fever virus (Waqar *et al*., 2023). Rift Valley fever virus can be easily inactivated by disinfectants like acetic acid, sodium hypochlorite and calcium hypochlorite; and can survive in cold temperature (Pal *et al*., 2012).

2.2. Transmission

Transmission predominantly occurs through the bites of infected mosquitoes, with *Aedes* and *Culex* species being key vectors (Wichgers *et al*., 2016). Importantly, infected animals serve as reservoirs for the virus, facilitating its transmission to mosquito vectors during blood feeding. As mosquitoes become infected, they play a crucial role in perpetuating the cycle by transmitting the virus to other animals or humans during subsequent bites. Transmission between animals by direct contact with infected tissues or fluids has been observed, together with iatrogenic route by use of infected needles used for vaccination, particularly in endemic regions with limited

economic resources (Pepin *et al*., 2010).

Rift Valley Fever virus primarily spreads through the bites of infected mosquitoes, with key vectors including species like *Aedes* and *Culex* (Wichgers *et al*., 2016). Infected animals serve as reservoirs, enabling the virus to pass to mosquitoes during blood feeding. Mosquitoes then perpetuate the cycle by transmitting RVFV to other animals or humans during subsequent bites. Additionally, direct transmission between animals through contact with infected tissues or fluids has been observed. In economically constrained endemic regions, transmission via contaminated needles during vaccination campaigns has also been documented. These diverse transmission pathways are crucial for designing targeted interventions to control RVFV spread among animal and human populations effectively (Pepin *et al*., 2010).

Human infections with Rift Valley fever virus can occur through inhaling aerosols containing infectious body fluids (Pal,2007), and the consumption of raw or unpasteurized milk is also recognized as a risk factor (WHO, 2023). The virus is transmitted from various mosquito species to both animals and humans, as well as from infected animals directly to humans (Pal,2007; Wright *et al*., 2019). There are 73 mosquito species across 8 genera in the family Culicidae known to be competent vectors for RVFV, with reports of trans-ovarian or vertical transmission (Lumley *et al*., 2017). Transmission between ruminants occurs primarily through mosquito bites, predominantly from the genera Aedes and Culex, but recent studies have also implicated species from the Anopheles and Mansonia genera, notably in regions like Madagascar and Kenya (Ratovonjato *et al*., 2011).

2.3. Clinical Sings in Animals

Rift Valley fever has been encountered in many species of animals, including antelope, buffalo, camel, cattle, goat, and sheep (Pal,2007; Pal *et al*.,2012). The incubation period of disease varies depending on the species affected. For newborn lambs, young calves, and pups, it typically lasts about 12 hours. Adult sheep, cattle, and goats have an incubation phase lasting one to three days, while in humans; it ranges from 4 to 6 days (Nielsen *et al*., 2020). Clinical symptoms in animals vary with age and species, with newborn lambs and young sheep being particularly susceptible. Endemic areas often experience abortion storms and high neonatal mortality rates. Infected animals can abort at any stage of gestation, with abortion rates ranging from 40% to 100% (Lubisi *et al*., 2023).

Young lambs affected by Rift Valley fever commonly present with symptoms such as anorexia, weakness, lymphadenopathy, and elevated body temperatures. They may also show serosanguinous or bloody mucopurulent nasal discharge, hemorrhagic or fetid diarrhea, melena, regurgitation, signs of abdominal pain, and increased respiratory rates. In adult sheep, the disease can manifest acutely or chronically, with some individuals showing no clinical signs while others experience fever lasting 1 to 3 days, anorexia, weakness, depression,

increased respiration, vomiting, abdominal discomfort, and bloody diarrhea. Pregnant sheep infected acutely have an almost 100% chance of miscarrying (Mansfield *et al*., 2015). Goats exhibit similar clinical signs to sheep, though their disease course can be more variable, with inconsistent viremia and symptoms following infection (Kwasnik *et al*., 2021).

Cattle generally exhibit lower susceptibility to the Rift Valley fever virus compared to sheep and goats (Wright *et al.,* 2019). In adult cattle with RVFV infection, symptoms typically include fever, dull coat, lacrimation (excessive tearing), nasal discharge, excessive salivation, anorexia, weakness, bloody diarrhea, reduced milk production, and high rates of abortion. Younger calves, however, are more vulnerable and often experience acute illnesses similar to those of other livestock species (Kwasnik *et al*., 2021).

2.4. Clinical Sings in Humans

The incubation period for Rift Valley fever ranges from 4 to 6 days (Pal,2007), typically presenting as a flu-like febrile illness that is self-limiting in most cases (Nielsen *et al*., 2020). Early symptoms are often nonspecific, contributing to a significant number of undetected cases. The overall case fatality ratio varies widely, estimated between 1% and 30% in specific endemic regions (Sado *et al*., 2022). Acute RVFV infection during pregnancy increases the risk of miscarriage (Baudin *et al*., 2016). Major complications in human cases include neurological issues such as headache, irritability, confusion, coma, and encephalitis, as well as visual hallucinations. Ocular complications may include retinitis, vision loss, and complete or partial blindness. Hemorrhagic manifestations are also observed, characterized by fever, myalgia, and severe bleeding from mucous membranes (Javelle *et al*., 2020).

2.5. Pathogenesis

Rift Valley fever virus replicates rapidly and reaches high concentrations in targeted tissues following entry through mosquito bites, percutaneous injury, or inhalation of oropharyngeal aerosols (Edward *et al*., 2011). After infection, the virus spreads from the initial site of replication to vital organs such as the spleen, liver, and brain. These organs can experience damage from the virus's pathogenic effects or Immunopathological processes, while healing may occur due to general and specific host responses. Lymphatic drainage transports the virus from the inoculation site to lymph nodes, where it replicates and enters the bloodstream, causing viremia and systemic infections (Ikegami, 2011). Severe cases often exhibit prominent hepatic necrosis, with necrotic lesions sometimes observed in the brains of patients with the less common encephalitic form of the disease. RVFV replication in cells is highly cytotoxic, suggesting that much of the cellular destruction during acute illness results from the direct viral killing of host cells (Mansfield *et al*., 2015).

2.6. Prevention and Control

There is currently no specific treatment for RVFV infection in humans or animals, with supportive therapy being the primary approach to care (Petrova *et al*., 2020). Prevention strategies are crucial and typically include immunizing animals in endemic areas, managing mosquito populations (vectors), monitoring climate changes, and implementing movement restrictions (Meegan *et al*., 2019). Vaccination of susceptible animals is an effective method to prevent RVFV transmission among amplifying hosts and, subsequently, vectors. Additionally, the use of insecticides to control mosquito populations and restrictions on livestock exports during Rift Valley fever epizootic periods are recommended (Pal, 2007). Various vector control measures can target mosquitoes at different stages of development. Pesticide applications can effectively manage adult mosquitoes through thermal fogging or ultra-low-volume spraying, directly targeting flying or resting adults (Bird and Nichol, 2012).

2.7. Economic impacts of Rift valley fever

Rift Valley fever imposes substantial economic burdens due to widespread animal abortions, deaths, and threats to food security, along with stringent trade restrictions (Aziz *et al*., 2018). The disease causes livestock market closures, high expenditures on disease control measures, and significant losses in livestock production, including meat and milk output. Livestock farmers are particularly affected by the high rates of animal mortality and abortion, leading to substantial stock losses, especially among young ruminants (Peyre *et al*., 2015). The disruption of herd dynamics can also result in long-term impacts, including decreased productivity that persists over several years or generations of animals. These economic consequences are influenced by various factors and have lasting effects on agricultural economics (Mburu *et al*., 2022).

Rift Valley fever outbreaks significantly impact the livestock industry and pose a considerable risk as a zoonosis, often spreading to human populations (Meegan *et al*., 2019). These risks are particularly pronounced in developing and transitional countries, where the public health infrastructure may be inadequate to support routine infectious disease surveillance, prevention, and control efforts, especially in areas where outbreaks occur every 5 to 15 years (Mahmoud *et al*., 2021).

2.8. Impacts of Rift Valley Fever on Human Health

Rift Valley fever is recognized as a significant zoonotic threat and classified as a high-consequence pathogen with the potential for international spread. It is listed as a "List A" disease by the OIE (2008). This

classification reflects its ability to cause severe disease outbreaks in both animals and humans. Occupational groups particularly at risk of infection include herders, farmers, farm workers, abattoir workers, veterinarians, and animal health workers, who are frequently in close contact with infected animals and bodily fluids (Pal *et al*., 2012).

Rift Valley fever virus spreads through contact with the blood or tissues of infected animals, both directly and indirectly. Direct contact includes activities such as performing veterinary surgical procedures, assisting with animal births, handling animal tissues during slaughter, butchering, or skinning, and disposing of fetuses and carcasses. Indirect transmission occurs through ingesting raw (unpasteurized or uncooked) milk from infected animals, inhaling aerosols generated during the slaughter or necropsy of infected animals, bites from infected mosquitoes (particularly Aedes species), and inoculation via wounds from contaminated instruments like knives or needles. Importantly, there have been no documented cases of RVFV transmission from person to person (OIE, 2008).

3. CONCLUSION AND RECOMMENDATIONS

Rift Valley fever poses significant challenges due to its impact on animal and human health, coupled with substantial economic consequences in affected regions. Rift Valley fever virus, transmitted primarily by mosquitoes during periods of heavy rainfall and flooding, affects domestic ruminants severely and can also infect humans, leading to a spectrum of clinical conditions from mild febrile illness to severe neurological, ocular, and hemorrhagic diseases. The disease's economic toll includes disruptions in livestock markets, high mortality rates among young animals, and losses in meat and milk production, exacerbating food insecurity and jeopardizing livelihoods in rural agricultural communities.

Based on the above conclusion, these recommendations are forwarded:

- Strengthening disease surveillance systems to monitor Rift Valley fever outbreaks and implementing early warning systems based on climate and environmental indicators can facilitate timely response and mitigation efforts.
- Emphasizing integrated vector management approaches, including targeted use of insecticides and environmental modification to reduce mosquito breeding sites, is critical for controlling RVFV transmission.
- An expanding and sustaining vaccination program for livestock in endemic regions is essential to prevent amplification of the virus in animal populations and subsequent transmission to humans.
- Promoting public awareness campaigns to educate communities, particularly at-risk occupational groups such as farmers, herders, and veterinary personnel, about

transmission risks and preventive measures can help to reduce human infections due to Rift Valley fever.

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All the authors contributed equally. They read the final version and approved it for publication.

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