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Review on economic significance and current diagnostic techniques on rift valley fever

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Abstract

Rift valley fever is an acute, mosquito-borne viral disease that has significant global threat to livestock marketing and on human health. The disease is caused by a virus of the genus *Phlebovirus* of family *Bunyaviridae*, a group of enveloped single stranded RNA viruses. A review of rift valley fever was made with the objective of organizing information on the epidemiology and management of rift valley fever, and on its economic impacts related to livestock marketing. Clinical disease is never been occurred in Ethiopia, serological tests are gotten IgM positive for rift valley fever. The transmission of rift valley fever is primarily by the bites of the mosquitoes of several species. Man acquires the infection from the infected animals and insect bites. Diagnosis is confirmed by polymerase chain reaction, isolation of virus, demonstration of antibodies in the sera and histopathology of the liver. Immunization of animals, destruction of mosquitoes and restriction on the movement of animals during epizootic can help in the control of rift valley fever.

Keywords: Economic impact; Rift valley fever; Transmission, Virus

1. Introduction

Rift valley fever virus (RVFV) is an arthropod-borne zoonotic disease responsible for widespread outbreaks in both humans and ruminants. RVF has a direct impact on livestock and human health as well as on trade. It is currently limited to Africa and parts of the Middle East but has the recognized potential to spread globally (Weaver, 2010). RVF is an acute, vector-borne, viral disease of mammals. It is caused by Rift Valley fever virus of the genus *phlebovirus*, family *bunyaviridae*. 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. In fatal cases and aborted foetuses, hepatitis with focal hepatic necrosis is a principal lesion. The clinical presentations and clinical case definitions for recognizing the disease (Mohamed *et al*., 2010). It can result in widespread febrile illness in humans, associated with severe and sometimes fatal sequelae in under one percent of cases.

Epizootics in livestock generally precede human epidemics; several major outbreaks have first been detected in humans, with livestock epidemics only retrospectively diagnosed. The close relationship between humans, animals and the environment in the epidemiology of RVF warrants a One Health approach to surveillance and response. The principal vectors of RVF are mosquitos: over 30 species from 12 genera have been implicated. The disease is cyclical in nature. Massive outbreaks in naïve populations result in high levels of immunity; populations regain susceptibility only after extended inter epidemic periods. Prolonged rains or changes in water management systems which lead to favourable conditions for vector multiplication trigger the epidemic cycle (Swanepoel and Coetzer, 2005). The disease is currently an economical concern because of the cost associated with preventive measures in endemic areas, monitoring for introduction of disease in neighboring unaffected areas, and trade restriction on import and export to and from countries (FAO. 2001). To understand RVF, make prevention and to be ready to take action in controlling, it is important to know the nature and epidemiology of the disease.

Therefore, the objectives of this seminar paper are, to review:

✓ Economic impacts and its risk factors of rift valley fever related to livestock disease

✓ Current diagnostic techniques on rift valley fever

2. Literature Review

Rift valley fever is a viral zoonotic that primarily affects animals but can also infect humans. The majority of human infections result from contact with the blood or organs of infected animals. Human infections have also resulted from the bites of infected mosquitoes. To date, no human-to-human transmission of RVF virus has been documented. The incubation period (the interval from infection to onset of symptoms) for RVF varies from 2 to 6 days. Outbreaks of RVF in animals can be prevented by a sustained programme of animal vaccination (WHO, 2010)

2.1. Etiology

Rift valley fever is caused by RVF virus which belongs to the family *Bunyaviridae* and the genus *Phlebovirus*. These are spherical virions with diameter of 80-120 nanometers and a host cell derived, bi lipid layer envelop through which virus coded glycoprotein spikes project (Davies, *et al.*, 2006). This single stranded Ribose Nucleic Acid (RNA) virus has a lipid envelope and two surface glycoproteins, G1 and G2. The genome has three segments: L (Large), M (Medium) and S (Small). RVF virus replicates in the mosquitoes and in the vertebrate animals. The liver, spleen and brain are the major sites of viral replication. The Virus is resistant in alkaline environments but inactivated at pH <6.8.The virus can be inactivated by disinfectants such as calcium hypochlorite, sodium hypochlorite and acetic acid; and be maintained for 8 years when stored below 0°C (Jeanmaire., 2011).

Currently, the distribution of RVF is restricted to the African continent, Madagascar, and Arabian Peninsula. It is especially prevalent in sub-Saharan Africa with major epizootics occurring every 5–20 years. RVFV is maintained in a cyclical pattern in Africa, resulting in significant epizootics of the disease during favorable climatic conditions. Unusually heavy rainfall and localized flooding predict ideal conditions for an outbreak (Pourrut *et al.*, 2010).

2.2. Epidemiology

2.2.1. Distribution and occurrence

Although Rift valley fever is still confined to the African continent it has great potentials for spread to other countries (Chevalier *et al.*, 2008). The disease is endemic in Southern and Tropical regions of many Eastern Africa countries, although an epidemic was reported in 2002 Saudi Arabia and Yemen. The main occurrence of the disease epizootics was observed in Eastern and Central Africa. The first thoroughly investigated epizootic begins in 1930 (Bird. *et al*., 2009). The incidence of RVF peaks in late summer. The virus is spread epidemically by many species of mosquitoes. Since its first outbreak among the sheep in 1931, the disease has been reported in several other species of animals and man. Countries with endemic disease and substantial outbreaks of RVF include Egypt, Gambia, Kenya, Madagascar, Mauritania, Mozambique, Namibia, Saudi Arabia, Senegal, South Africa, Sudan, Yemen, and Zambia (KonradSK, *et al.*, 2012).

The cyclic epidemics have occurred at 5-20 years intervals in drier areas. In the periods between epidemics, the virus is believed to be dormant in eggs of the mosquitoes. Many countries like Angola, Botswana, Burkina Faso, Cameroon, Chad, Congo, Ethiopia, Gabon, Guinea, Malawi, Mali, Niger, Nigeria, Somalia, Tanzania and Uganda are known to have some cases, periodic isolation of virus, or serologic evidence of RVF (Chevalier *et al.*, 2008).

2.3. Host range and susceptibility

Natural infection due to RVF virus has been recorded in antelope, buffalo, camel, cattle, goat, monkey, rodents, and sheep besides man. Significant mortality and morbidity due to RVF have been reported in sheep, cattle and man. Several species of domestic, pet, farm and laboratory animals are susceptible to RVF virus. The kids, lambs, puppies, kittens, hamsters and mice are highly susceptible to RVF virus. Amphibians and reptiles are resistant to RVF virus (Davies, *et al.*, 2006).

2.4. Source of infection

A pronounced viremia occurs in infected animals for about a week and facilitates the spread of the disease of biting insects. During viremic period blood, tissue of affected animals, aborted fetus and fomites are source of infection (Faye, *et al.*, 2003).

2.5. Morbidity and mortality

Young animals, such as lambs, kids, puppies, and kittens are considered as extremely susceptible with mortality of 70%-100%. Sheep and calves are considered as highly susceptible with mortality rates between 20%-70%. Adult cattle, goats, buffaloes, and humans are considered as moderately susceptible and mortality rate is typically less than ten percent; for humans the case fatality rate is typically less than one percent. Equines, pigs, dogs and cats are categorized as resistant and infection is unapparent (Faye, *et al.*, 2003).

2.6. Mode of transmission

It was founded that the virus is transmitted transovarially among flood water *Aedes* species mosquitoes. The virus survives for long periods in mosquito eggs laid at the edge of usual dry depression, called dambos, which are common through grassy plateau regions. When the rain comes and these dambos flood, the egg hatch and affected mosquitoes emerge and infect nearby wild and domestic animals. Direct and indirect transmission can occur via aerosol, contact with infected placenta or aborted fetus, fomites or mechanical transport on the mouth part of flies (Madani, *et al*., 2003).

Animals and man get infection following the bites of many species of mosquitoes. The virus survives for very long periods in the mosquito eggs. Cattle and sheep are primary amplifiers of the virus. The capacity of RVF virus to transmit without the involvement of an arthropod vectors raises concern over the possibility of the virus for its importation in to non-enzootic areas through contaminated materials, animal products, viremic humans or no livestock animal species. Low concentration of RVF virus in the milk of sick animal may pose health risks to man if the milk is consumed raw or unpasteurized (Chevalier, *et al*., 2004). Humans have the potential to introduce RVF virus through mosquitoes bite to animals in uninfected areas (Anyamba, *et al.*, 2009).

2.7. Risk factors

The incidence of the disease varies with size of the vector population and it is greatest in season of heavy rainfall. This allows the vector population to breed in surface water in normally dry areas (Coetzer, *et al.*, 1982). Most indigenous livestock species in Africa demonstrate a high level of resistance to the disease. A high degree of herd immunity arises in locations where infections are most intense and it was one of the factors which contribute to the abatement of enzootics. Because of the massive immunity produced in recovered animals which is also transferred passively with the colostrums from the dam to calf and from the ewe to lambs, enzootics appear only in interval of 4-7 years (Faye, *et al.*, 2003).

2.8. Clinical signs

Rift valley fever is characterized by high abortion rates and high mortality in neonates usually occurring after periods of heavy rainfall. Pathology typically finds hepatic necrosis, splenomegaly, and gastrointestinal hemorrhage (Pepin, *et al*., 2010). In cattle: Calves experience fever (104–106°F/40–41°C), inappetence, weakness, depression, diarrhea, and jaundice. Adults often experience inapparent infection; clinical disease is characterized by fever lasting 24–96 hours, dry and/or dull coat, lachrymation, nasal discharge, excessive salivation, anorexia, weakness, bloody diarrhea, low milk yield, and high abortion rates in pregnant cows (Ikegami, *et al*., 2011). In sheep and goats: Newborn lambs (less than 2 weeks of age) experience biphasic fever (40–41°C), anorexia, weakness, abdominal pain, rapid respiration, and death within 24–36 hours. Lambs (over 2 weeks of age), adult sheep, and goats experience fever lasting 24–96 hours, anorexia, weakness, depression, increased respiratory rate, vomiting, bloody diarrhea, mucopurulent nasal discharge, jaundice, and abortion rates approaching 100 percent. In humans: RVF presents in humans as influenza-like syndrome characterized by fever (37.8–40°C), headache, myalgia, weakness, nausea, and light sensitivity. Complications can arise and result in retinopathy, blindness, meningoencephalitis, hemorrhagic syndrome with jaundice, petechiae, and death (Bird, *et al*., 2009).

2.9. Pathogenesis

Rift valley fever virus replicates rapidly and to very higher titer in target tissues after entry by mosquitoes bite, percutaneous injury or through the oropharynx through aerosols (Edward, *et al.*, 2011). After infection the virus spread from the initial site of replication to critical organs such as the spleen, liver and brain which are either damaged by the pathogenic effects of the virus or immunopathological mechanisms, else there is recovery mediated by nonspecific and specific host response. 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 (Ikegami, *et al*., 2011).

2.10. Pathologic lesions

Hepatic necrosis is the primary lesion observed in Rift valley fever. In aborted fetuses and neonatal animals, particularly the lambs and calves, the liver is soft, enlarged, friable and yellowish brown to dark in color. In addition, the edema and hemorrhages in the wall of gall bladder, hemorrhagic enteritis, enlarged edematous peripheral and visceral lymph nodes, widespread cutanous hemorrhages, accumulation of blood stained fluids in the body cavities and extensive subcutaneous and serosal hemorrhages are also observed. The rapid decaying of the carcass may be a consequence of the severe liver damage. In lambs there is a focal to diffuse coagulative necrosis of hepatocytes in the affected liver (USDA. 2011).

3. Diagnosis of rift valley fever

3.1. Clinical diagnosis

Affected animals show fever (40-42°C), anorexia, depression, weakness, mucopurulent nasal discharge, vomiting, jaundice and hemorrhagic diarrhea (Swanepoel, *et al*., 2004).

3.1.1. Field diagnosis

Rift valley fever should be suspected when abnormally heavy rains fall is followed by the wide spread occurrence of abortion and mortality among new born animals characterized by necrotic hepatitis and when hemorrhages and influenza like disease are seen in people handling animals or their products (Kahen, 2005).

The field veterinarian can suspect RVF if he/she encounters high abortion rates possibly approaching 100% among the cows and ewes; very high mortality approximately 100 % in calves and lambs of less than 7 days of age, extensive liver lesions in aborted fetuses and neonatal animals, an influenza like disease in man particularly in individual associated with livestock and occurrence of disease during a period of high insect activity (Davis, 2003).

3.1.2. Differential diagnosis

Differential diagnoses in animals include: blue tongue, heart water disease, Nairobi sheep disease, ephemeral fever, brucellosis, Wessel borne disease, pest des petites ruminitis, foot and mouth disease. Nairobi sheep disease has no hepatitis and does not occur in new born lambs. In case of bluetongue no hepatitis and lesions on mouth and foot (coronitis) are common. Serous fluid in body cavities and neurological signs are common in heart water disease. In ephemeral fever there is recumbence (muscle weakness), rapid recovery and is not commonly occur in sheep and goats, while brucellosis does not occur in relation with heavy rain fall. Wessel borne disease is rare viral disease and less severe than rift valley fever (Gerdes, 2004)..

3.2. Laboratory diagnosis

There are several methods by which RVF virus can be diagnosed in clinical laboratories. These clinical laboratory methods include:

3.2.1. Isolation and identification of causative agent

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 (Ochei, *et al.* 2000).

The clinical specimens such as the liver, spleen, brain, lymph nodes, kidney, heart, and blood should be collected aseptically in sterile container for virus isolation. In case of an autolysed fetus, the brain is a good specimen to be submitted on ice to the laboratory for diagnosis. Several types of cell cultures such as Baby Hamster Kidney (BHK), African green monkey kidney (Vero), Chicken Embryo Reticulum (CER), or primary kidney and testis cell cultures of lambs and laboratory animals like mice and hamsters can be employed for the isolation of virus (Swanepoel, *et al*.,2004).

3.2.2. Serologic diagnosis

Detection of specific viral antibody and their quantification at various stages of the disease is an important tool for the diagnosis of many viral diseases. Because of its broad geographic distribution and its explosive potential for invading new areas where livestock husbandry is extensive, the laboratory confirmation of the presence of RVF virus is treated as a diagnostic emergency (OIE. 2008).

Two sera samples at an interval of 30 days should be obtained to demonstrate antibodies against RVF by Enzyme Linked Immune Sorbent Assay (ELISA), Agar Gel Immune Diffusion (AGID), Hemagglutination (HI) and virus neutralization methods. The virus antigen can be detected by Reverse Transcriptase Polymerase Chain Reaction (RT-PCR). It is a very specific and sensitive molecular tool for the diagnosis of RVF in the early phase of disease. PCR used for rapid diagnosis for antigen detection and used to detect RVF virus in mosquito pools. RT-PCR followed by sequencing of the nucleocapsid protein-coding region has been used in phylogenetic analysis (OIE. 2008).

3.2.3. Virus neutralization (the prescribed test for international trade)

Cannot differentiate presence of antibodies of naturally infected animals from animals vaccinated with Rift valley fever vaccine; detects antibodies against Rift valley fever virus in the serum of a variety of species highly specific and will record the earliest response. These tests can only be performed with live virus; thus not recommended for use outside endemic areas or in laboratories without appropriate biosecurity facilities and vaccinated personnel (OIE. 2008).

3.2.4. ELISA

Can be performed with inactivated antigen and can therefore be used in RVF-free countries. Cross-reactions may occur between RVF virus and other *Phleboviruses*. Use of inactivated whole virus or mouse liver antigens has recently been replaced by recombinant nucleocapsid protein as antigen. IgM capture ELISA allows diagnosis of a recent infection. Hemagglutination inhibition can be performed with inactivated antigen and can therefore be used in RVF free countries. It employed with great confidence in non-endemic areas (WHO, 2009).

3.3. Control and prevention

4.4.1. Vaccinations

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. The live attenuated Smith burn vaccine induces lifelong immunity in sheep and goats. The Smith burn vaccine has a potential for reversion, so it is not recommended for widespread use in non-endemic countries or during outbreaks. The inactivated vaccine does not confer long term immunity and thus requires booster vaccination and annual revaccination for continued protection against infection. The inactivated vaccine is recommended for use in pregnant animals and in RVF free countries experiencing outbreaks (WHO, 2009).

4.4.2. Vector control

Mosquitoes are the most important way that RVF is spread. It is only the female mosquito that feeds on blood as she needs the protein to produce eggs. Mosquitoes will lay their eggs on or near the edge of water. The mosquito eggs will hatch into larvae (also known as wigglers) which turn into pupae (also known as tumblers). The larvae and the pupae need to live in water to survive. The pupae will change into adult mosquitoes (FAO. 2005).

4.4.3. Control of mosquito egg laying sites

Mosquitoes can lay their eggs any place that can hold water. This includes: ponds, old tires, tarps, tree holes, bird baths and flower pots. This is the best way to control mosquitoes since they lay eggs in specific areas and these areas can be managed (FAO. 2005).

4.4.4. Control of mosquito larvae (wigglers)

Mosquito larvae need to live in water to survive. They can be found in any amount of standing water including ponds, old tires, tarps and bird baths. Since mosquito larvae remain in the same water where they hatched from eggs, control of this stage focuses on continued management of mosquito egg laying areas (Chengula, *et al.,* 2014).

4.4.5. Control of mosquito adults

This is the least effective way to control mosquitoes. Attempting to control adult mosquitoes can be difficult and costy. Control of adult mosquitoes focuses on the use of pesticides (Pfeffer, 2010).

4.4.7. Reducing host exposure to biting *Aedes*

The movement of stock from low lying areas to well drain and winds wept pastures of higher altitude, or confinement of animals to mosquito proof sheds may be measures of management to reduce the incidence of RVF. The breeding management may also take in to account the seasonal activities of vectors and prevents the lambing and or calving season during the rainy season (Anyamba, 2001).

4.4.8. Prevention of introduction of rift valley fever

Movement control refers to activities regulating the movement of people, animals, animal products, vehicles, and equipment in an area subject to certain criteria. Movement control is accomplished through a permit system that allows entities to make necessary movements without creating an unacceptable risk of disease spread (Chevalier, 2010). Quarantine refers to imposing restrictions on entering or leaving a premise, area or region where disease exists or is suspected. Quarantine stops the movement of infected animals, contaminated animal products, and fomites from infected, contact, and suspect premises. Infection can be introduced in to an area free of RVF by infected animals, animal products and insects (*Aedes*) (Anyamba, 2001).

5.2. Rift valley fever in Ethiopia

In the Horn of Africa, the Somali region of Ethiopia is one of the most active livestock trading areas, and various sources estimate that 60-80% of Somalia's livestock exports originate from this region of Ethiopia through a largely informal cross border trade. RVF clinical disease has never been reported in Ethiopia. RVF was reported to OIE following positive serological tests but no clinical disease. The geographical localization of the country, associated with large commercial ruminant trade and pastoralist's movement makes Ethiopia at risk for RVF occurrence (Pfeiffer, 2005).

In 2009/10 National Animal Health Diagnostic and Investigation Center (NAHDIC) in collaboration with regional veterinary laboratories has collected a total of 14,328 serum samples for RVF, foot and mouth disease, pest des petites ruminitis and brucellosis. The overall prevalence of the diseases was 0%, 11%, 57% and 0.4%, respectively (FAO. 2005). Rift Valley fever is one of the most important diseases that affect the export of live animals and meat to prime markets in the Middle East countries. Since 1997/98, Ethiopia has faced a total of three bans as a result of epidemic situations of the disease in Kenya and Somalia. Although clinical cases of the disease have never been reported in Ethiopia, 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 (Chevalier, 2010).

5.3. Economic impacts of rift valley fever

The economic impacts of RVF include death of animals and abortion of animal trade, devastating food security and cost of control. Pastoral communities relying on a livestock economy are highly vulnerable to the threat of disease to their livestock such as RVF (Linthicum, *et al.*, 1985). Moreover in the context of the Horn of Africa, pastoralists who represent 15-20 million people in Djibouti, Eritrea, Ethiopia, Kenya, Somalia and Sudan have turned to a market integration and international trade orientation. This has led to new development opportunities but also to new economic threats, by increasing interdependence with the international economy (Pfeiffer, 2005).

The first reported direct socio-economic impact of RVF was on livestock producers due to high levels of mortality and morbidity in animals. This represents an important loss of stock, especially in young ruminants. In addition, the disturbance on herd dynamics could result in production losses lasting several years or even several animal generations (long term effects). These effects are perceived over the long term and are subject to the combined influence of other economic mechanisms besides the strict herd dynamics (Pfeiffer, 2005).

5. Impacts of Rift Valley Fever on Livestock Marketing

In Africa, pastoralist plays an important role in national economies. In particular, the export of livestock from the pastoral communities to the Middle East is of vital economic importance as millions of animals are exported each year, particularly during the religious festival periods.RVF virus is 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 (Shoemaker, *et al.*, 2002).

Trans-boundary diseases are diseases that are significant in economic trade and or food security importance for a considerable number of countries, which can easily spread to other countries and reach epidemic proportion; and where control or management, including exclusion requires cooperation between several countries (Chevalier, *et al*., 2011). As a list 'A' disease among the Office International Des Epizootics (OIE) classification of contagious diseases being threats for international economy, RVF is a major stake for the establishment of nontariff barriers. The ban on livestock imports from the Horn of Africa was apparently imposed for public health reasons because of concern that slaughter of RVF virus infected livestock could result in disease transmission to people. OIE regulations refer two types of country status with regard to RVF: free and non free countries, given the present status and the animal health situation in Ethiopia, the possibility of Ethiopia being declared free from RVF is considered a major effort not attainable in the near future (Shoemaker, *et al.*, 2002).

6. Conclusion and Recommendations

Rift Valley fever is economically important disease. In addition to its impact on animal health the impact it results due to import and export restriction is significant particularly in those countries which livestock contributes great share in their economy. As rift valley fever needs insects, a mosquito, for its life cycle and transmission, its epidemics has cyclical occurrence. The disease affects different species of animals including humans. Immunization and vector control are the main strategies to reduce the incidence of RVF. It is considered as an occupational disease of livestock handlers, dairy farmers, abattoir workers and veterinarians. Based on the above conclusions the following recommendations are forwarded:

✓ Sub Saharan countries and their trade partners should collaborate and consider cost effectiveness analysis for planning and monitoring of rift valley fever to benefit the most out of the livestock industry.

✓ Cyclical occurrence should be considered while planning surveillance program of rift valley fever.

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