

Rift valley fever- an emerging zoonoses

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Abstract

Rift Valley fever (RVF) is an emerging and devastating disease of small ruminant and the occurrence of antibodies to RVF virus in sheep and goats was first reported from Rajasthan state in 1995 followed by an outbreak among sheep was reported from Tamil Nadu state. This mini review highlighted about the morphology about the virus, virus replication in vector and spreading to the other animals, importance of the vector in virus propagation and disease transmission, various routes of transmission, clinical features of the disease, epidemiology of the disease, diagnostic methods and prevention and control measure. The review mainly focuses on the status of the disease in small ruminant and humans particularly in India. The disease is highly infectious particularly in small ruminant causing heavy mortality and thus economic losses to the farmers. However, very limited information of the disease is available in India. Therefore, there is need for an effective surveillance of the disease, virus propagation and transmission of the disease from different pockets of the country.

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Received: 24/04/2013

Revised: 27/09/2013

Accepted: 27/09/2013

Keywords: Emerging Pathogen, epidemiology, RVFV, zoonoses

Introduction

Rift Valley fever has long been a devastating disease of ruminant livestock in Africa. It is a fever-causing disease that affects livestock (including cattle, buffalo, sheep, and goats) and humans in Africa. It is named after a trough stretching 4,000 miles from Jordan through eastern Africa to Mozambique. It kills livestock and induces abortion in pregnant ewes and cows. At the time of such epidemics, a few cases of a nonlethal dengue-like illness were observed in people who were exposed to the animals. The Rift Valley virus was first isolated in 1931 in livestock on a farm in Kenya. The most notable epizootic occurred in Kenya in 1950-1951 and resulted in the death of an estimated 100,000 sheep. In 1978, the virus was detected in Egypt and caused a large outbreak of

illness in animals and humans. In 1977, an epizootic occurred of large size in the Nile Valley which hundreds of thousands of livestock cases and large numbers of humans. The virus was detected in eastern Africa in the late 1980's and caused hundreds of human deaths. In India, occurrence of antibodies to RVF virus (or a closely related virus) in sheep and goats was first reported from Rajasthan state in 1995. Subsequently, an outbreak of RVF-like disease among sheep was reported from Tamil Nadu state.

Virus

RVF is considered to be one of the most important viral zoonoses in Africa. The viral agent is an arbo virus which belongs to the phle-

bovirus genus in the Bunyaviridae family. This family of virus comprised more than 300 members grouped into 5 genera: Orthobunyvirus, Phlebovirus, Hanta virus, Nairo virus and Tospo virus. Several members of this family are responsible for fatal hemorrhagic fevers: RVFV (Phlebo virus), Cremerian Congo Hemorrhagic fever virus (Nairo virus), Hantaan, Sin Nombre and related viruses (Hanta virus), and recently Garissa, now identified as Ngri virus (Orthobunya virus). The nucleoprotein N is the most abundant component of virion, numerous copies of N associate with the viral RNA genome and formed by the base-paired RNA sequences at the 3' and 5' termini. These structures play critical role in transcription and replication (Le May *et al.*, 2005).

Vector

When a competent mosquito ingest viremic vertebrate blood, virus infect midgut epithelial cells and replicates, then disseminate to other tissues including salivary glands and ovaries. The virus then transmitted to the next vertebrate host horizontally via bite and vertically to the mosquitoes offspring. Not all mosquitoes that ingest virus become infected or if infected, transmit virus. Gut escape barrier and salivary gland infection barriers prevents arbovirus passage and thus transmission. Midgut basal lamina pore sizes are significantly smaller than arboviruses and ultra structural evidence suggest that midgut tracheae and trachioles may provide a means for viruses to circumvent this barrier. The basal lamina may prevent access to mosquito cell surface virus receptors and help explain why anopheline mosquitoes are relatively incompetent arbovirus transmission when compared to culicines (Romoser *et al.*, 2005).

The virus was isolated from the flood water mosquitoes *Aedes vexans* and *A. ochraceus* by Fontenille *et al.* (1998). In 1974 and 1983, the virus had been isolated from *A. dalzieli*. Although these vectors differ from the main vector in East and South Africa. Four of 14 species of rodents were found to have anti-RVF virus antibodies: *Rattus rattus* (one positive of 2

tested), *Mastomys huberti* (13.5%), *A. niloticus* (4.3%), *M. arthroleucus* (2.4%) (Gora *et al.*, 2000).

Transmission

The virus can be transmitted to humans by direct or indirect contact with the animal secretions, handling of animal tissues during slaughtering and disposal of carcasses or fetuses. It can also be transmitted through inoculation of virus into wound from an infected knife or through contact with broken skin. Aerosols transmission is also possible during the slaughtering of infected animals.

Certain occupational groups such as farmers, slaughterhouse workers, laboratory workers and veterinarians are therefore at higher risk of infection. Humans may also become infected with RVF by ingesting the unpasteurized or uncooked milk of infected animals. Human infections have also resulted from the bites of infected mosquitoes, most commonly the *Aedes* mosquito and by hematophagous (blood-feeding) flies. However, no human-to-human transmission of RVF has been documented.

Among animals, the RVF virus is spread primarily by the bite of infected mosquitoes (mainly *Aedes* spp.), which can acquire the virus from feeding on infected animals. It has been reported that the virus has capability to transmit transovarially in female mosquito leading to new generations of infected mosquitoes and the eggs of these mosquitoes can survive for several years in dry conditions. Thus, the virus is continuously present in enzootic foci. During periods of heavy rainfall, larval habitats frequently become flooded enabling the eggs to hatch and the mosquito population to rapidly increase, spreading the virus to the animals on which they feed.

Clinical Features

After a brief incubation period of 2-6 days, fever, severe headache, retro-orbital pain, photophobia, and generalized myalgia begins. Patients tend to progress to one of three final complications: mild encephalitis, retinitis,

or hemorrhagic fever. The disease resembles influenza-like illness in humans and causes fever, chills, headache, backache, myalgia and hepatitis. Some patients may develop neck stiffness, sensitivity to light, loss of appetite and vomiting which in its early stages, may be mistaken for meningitis. Very few percentages of patients develop a more severe form of the disease which usually appears as one or more of three distinct syndromes: ocular (eye) disease (0.5-2% of patients), meningoencephalitis (less than 1%) or haemorrhagic fever (less than 1%). However, in animals, it is characterized by fever, anorexia, diarrhoea, hepatitis and abortion of pregnant ewes.

Epidemiology

The natural vertebrate reservoir of the Rift Valley fever virus has not yet been precisely identified but is suspected to be one or several wild ungulates. The virus remains in a silent enzootic cycle for many years, and then, during a period of heavy rainfall, it explodes in epizootics of great magnitude among sheep and cattle. During such epizootics, the virus is transmitted by many species of mosquitoes and may also be transmitted by fomites, direct contact and by arthropods. This epizootic cycle is closely tied to the ecological niche of the *Aedes* mosquitoes. These mosquitoes hatch from dormant eggs in dry depressions located in the grassy plateau regions of sub-Saharan Africa with abundant rainfall and are infected transovarially with the virus. The *Aedes* mosquitoes, thus being the epizootic which is maintained by other species of mosquitoes. Age of the animals has also been shown to be a significant factor for susceptibility to the severe form of the disease. Over 90% of lambs infected with RVF die, whereas mortality among adult sheep can be as low as 10%. The rate of abortion among pregnant infected ewes is almost 100%.

Rift Valley fever is most common in the livestock-raising regions of eastern and southern Africa. The virus was first identified during an investigation into an epidemic among sheep on a farm in the Rift Valley of Kenya in 1931. Since then, outbreaks have been reported in sub-

Saharan in Madagascar and North Africa. The first epidemic of Rift Valley fever in West Africa was reported in 1987. It was linked to construction of the Senegal River Project, which caused flooding in the lower Senegal River area. In late 1997, after exceptionally heavy rains, an epidemic resulted in the deaths of at least 300 people and large numbers of animals in remote parts of northeastern Kenya, southern Kenya, and southern Somalia. Later in September 2000, RVF virus spread through Arabian Peninsula and cause 2 simultaneous outbreak in Yemen and Saudi Arabia (Flick, and Bouloy, 2005), marking the first reported occurrence of the disease outside the African continent and raising concerns that it could extend to other parts of Asia and Europe. During the 2003 rainy season, the clinical and serological incidence of rift valley fever was assessed by Chevalier *et al.* (2005) in small ruminants herds living around temporary ponds located in the semi-arid region of the Ferlo, Senegal.

Recently, large numbers of outbreaks of RVF have been reported from various countries especially Kenya and Somalia. In November 2006, due to heavy rain fall RVF outbreak occurred in North eastern and Coast province of Kenya. Later, in January 2007, 75 people died and 183 got infected in the same region (Anonymous, 2007a), which was then spread to the Somalia killing 14 people (Anonymous, 2007b). In January 2007, Nyama Choma (Roast meat) was believed to be spreading the fever cases in Kenyan capital Nairobi. In March 2007, the Kenyan government declared RVF as having diminished drastically after spending an estimated 2.5 Million in Vaccine and deployment costs, It also lifted the ban on cattle movement in the affected areas. In November 2007, 125 cases including 60 deaths have been reported from White Nile, Sinnar, and Gezira states in Sudan. More than 25 human samples have been found positive for RVF by PCR or ELISA (WHO, 2007).

In India, very limited work has been carried out on Rift Valley Fever. However, occurrence of antibodies to RVF virus (or a closely related virus) in sheep and goats by -

haemagglutination inhibition (HI) and ELISA was first reported from Rajasthan state in 1995 by Joshi *et al.* (1995). However, Kharole *et al.* (1982) reported abortions in goats resembling those caused in Rift Valley Fever on the basis of clinical symptoms at University farm of Haryana Agriculture University, Hissar. Subsequently, an outbreak of RVF-like disease from 6 flocks of sheep was reported from Veerapuram Village in the Chennai-MGR district, with the first death in August 1994 and the disease spread to other flocks and identified on the basis of the clinical signs, high mortality, abortions and liver lesions (Manohar *et al.*, 1995). During epizootic, no virus was isolated from sheep but the detection of haemagglutination inhibition and anti RVF IgG antibodies in sheep sera (convalescent and survey) was suggestive of an RVF-like illness (Joshi *et al.*, 1998). However, during the post-epizootic period a male lamb died of similar clinical features and the spleen was immediately collected and processed further for confirmation by Yadav *et al.* (2004). By Electron microscopic observations, they found that the virus particles resembling flaviviruses, however, RT-PCR gave negative results with RVF specific primers. There is a need to carefully monitor this newly emerging virus infection in our country.

Diagnosis

ELISA sensitivity ranges from 99.47% (humans) to 100% (sheep, buffalo and camels) Paweska *et al.* (2005). The specificity ranges from 99.29% (sheep) to 100% (camels). Compared to virus neutralization and haemagglutination inhibition tests, the ELISA was more sensitive in detection of the earliest immunological response in experimentally infected and vaccinated sheep. The virus itself may be detected in blood during the early phase of illness or in post-mortem tissue using a variety of techniques including virus propagation (in cell cultures or inoculated animals), antigen detection tests and RT-PCR.

Prevention and Control

Most of the human cases of RVF are relatively mild and of short duration. Therefore,

no specific treatment is required for these patients. However, for more severe cases, the predominant treatment is general supportive therapy.

Live attenuated and formalin inactivated Rift Valley fever vaccines are available for livestock immunization. These live attenuated RVF vaccines (Smithburn strain) in sheep are effective and inexpensive, but they cause abortion in pregnant ewes and inactivated vaccines produced in cell cultures are effective but costly (Barua *et al.*, 2004; Vaid *et al.*, 2004). Due to the large number of livestock, however, prevention of outbreak is unrealistic. No commercial human vaccine is available. However, US Army successfully developed an improved version of inactivated RVF vaccine, TSI-GSD-200. Three s/c doses (0, 7 and 28 days) of 0.5ml of TSI-GSD-200. A total of 540 vaccine (90.3%) initially responded (group A) with an 80% plaque reduction neutralization antibody titer (TRNT-80) of $> \text{ or } = 1:40$. Thirty three of 44 (75%) initial non responders were converted to responder starter after the first booster, which is a lower rate than that of group A ($P < 0.001$). Kaplan-Meier analysis showed 50% probability of group A members maintaining a titer of $> \text{ or } = 1:40$ for appr. 8 years; whereas, group B had a 50% probability of maintaining a titer for only 204 days. Minor side effects to TSI-GSD-200 were noted in 2.7% of all vaccines (Pittman *et al.*, 1999).

Conclusion

Due to poor diagnostic facilities, similar kind of symptoms with other diseases like dengue and Japanese encephalitis and availability of virus in limited pockets of Rajasthan and Tamil Nadu, the importance to the deadly disease has not been given. Thus, the disease has been neglected in India. At any point of time, the virus can emerged and spread to longer distance within a short span of time, which may leads to heavy morbidity and mortality among the livestock (especially sheep and goat) as well as humans. Therefore, people should aware about the disease as the virus

spread rapidly by many ways, trans-ovarially transmitted to the next generation in mosquitoes and stable for longer duration, proper preventive measure at proper times needs to be implemented. The spread of disease can be effectively controlled by implementing Sanitary and Phytosanitary (SPS) Agreements. During an outbreak, mosquito control and implementation of safer animal handling practices could help to decrease the outbreak. Active animal health surveillance system is also required to detect new cases in order to provide early warning for veterinary and human public health authorities.

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