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Kyasanur forest Disease: A review article

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Abstract

Kyasanur forest disease (KFD) is a emerging tick borne zoonotic disease caused by Kyasanur Forest Disease Virus (KFDV), discovered in 1957, which belongs to member of the genus Flavivirus and family Flaviviridae. It causes acute febrile hemorrhagic illness in humans and in two species of monkeys the black faced langur (*Presbytis entellus*) and the bonnet macaque (*Macaca radiata*) particularly in southern part of India. The disease is transmitted to monkeys and humans by infective tick *Haemaphysalis spinigera*. Seasonal outbreaks are expected to occur during the months of January to June. The aim of this paper is to briefly summarize the epidemiology, mode of transmission of KFD virus, clinical findings, diagnosis, treatment, prevention and control of the disease.

Keywords: Kyasanur forest disease, zoonotic disease, flavivirus, ticks, monkey, humans

Introduction

Kyasanur Forest disease (KFD), a tick-borne viral disease, was first recognized in 1957 in Shimoga District, India, when an outbreak in monkeys in Kyasanur Forest was followed by an outbreak of hemorrhagic febrile illness in humans [1]. KFD is exclusive to 5 districts (Shimoga, Chikkamagalore, Uttara Kannada, Dakshina Kannada, and Udupi) of Karnataka State and occurs as seasonal outbreaks during January–June [2, 3]. It is also termed locally as Monkey Disease or Monkey Fever because of the fact that the disease was first isolated from monkeys [1]. The disease is seen in both wild primates and humans living near forested areas. The virus KFD belongs to Russian Spring Summer Encephalitis group, an RNA genome virus of family Flaviviridae. Kyasanur Forest disease is a zoonotic illness, with humans as incidental hosts. The natural cycle involve infection of a non- human vertebrate host (mammal or bird), transmitted by *Haemaphysalis* ticks [4]. Ticks can become infected at any stage in their life cycle and virus is passed to succeeding tick stages during trans-stadial transmission, as well as trans-ovarially to progeny of adult ticks. Accordingly, tick species may act as the reservoir and vector for the disease. Black- faced langur, bonnet macaque, grey langur, humans, rodents (shrews, forest rat), ground dwelling birds, flying squirrels, Malabar giant squirrels, three striped squirrels and bats have been among the host species ranges of KFDV [5].

Most of the human infections with KFDV occur in the drier months of the year, with peaks in March and April and the number of cases is variable. Around 400–500 cases of KFD are reporting from India every year [6]. In recent years, this disease has crossed the state borders and reported from three neighbouring states of Karnataka, viz., Kerala, Goa and Maharashtra with human cases and monkey deaths. Kyasanur Forest disease virus infection causes severe febrile ailment in some monkeys [4]. In humans, the disease causes high incidence of acute febrile illness progressing to haemorrhages with mortality in 2–10% of the cases [7,8]. Prompt laboratory investigations and symptomatic treatment should be carried for KFD as there is no specific treatment [9]. This review highlights the etiology, transmission, clinical signs, diagnosis, treatment and prevention and control measures.

Etiology

The Kyasanur Forest disease virus (KFDV), belongs to the family Flaviviridae and genus Flavivirus. The virus was initially suspected as a Russian spring- summer (RSS) complex of viruses, since isolates from monkeys and Humans showed relatedness to this virus. The KFDV has been isolated from dead monkeys, humans and ticks. KFDV has a genomic organization consisting of a single-stranded RNA molecule of nearly 11 kb encoding a Polyprotein which is cleaved into three structural and seven non-structural proteins [10].

Mode of transmission

In the natural transmission cycle of KFD, Ticks act as vectors and main reservoirs of KFDV [11]. The *Haemophysalis* ticks transmit the infection to a vertebrate host that is non-human such as bird or mammal [12]. The *H. spinigera* and *H. turturis* are the two main vector species and are found to inhabit the forest floors and vegetation and also infest various small mammals and birds. KFD is a zoonotic disease, in which humans play no major role in the infection transmission but acts as dead-end hosts [11]. In enzootic state, KFD virus circulates through small mammals such as rodents, shrews, ground birds and tick species. Out of this mainly rodents, have been considered as reservoirs for the KFD.

KFD is often fatal among nonhuman primates and is known to affect two South Indian species; *Macaca radiata* (bonnet macaque) and Langurs (e.g., Gray langur) [2]. Large animals like goats, cows and sheep may become infected with KFD but play a limited role in the transmission of the disease due to insignificant viremia in them. These animals provide the blood for ticks and it is possible for infected animals with viremia to infect other ticks [13, 14].

Clinical signs and symptoms

In humans, the incubation period of KFD is estimated to be about 2 to 7 days after tick bites or exposure [15, 16]. The onset is sudden followed by headache and fever which rapidly rises to 104°F. The clinical symptoms of KFD pass through various stages. i.e. a prodromal stage lasting 12 days or longer characterized by high grade fever with chills, frontal headache, myalgia, photophobia, severe prostration, hypotension and hepatomegaly [17]. This stage is followed by hemorrhagic stage characterized by epistaxis, haemoptysis and gastrointestinal bleeding including melena. Relapse of the symptoms are often observed after 1 to 2 weeks of the first febrile period, last for 2 to 12 days. KFD may be biphasic in presentation. The relapse phase displays same symptoms as the first phase and in addition neurological symptoms such as altered sensorium and reflex abnormality are often seen. Pulmonary haemorrhage and massive gastrointestinal haemorrhage are terminal complications that can cause death [18, 19]. The convalescent phase is generally prolonged, maybe up to 4 weeks. KFD patients in convalescence can be lethargic for weeks and often results in tremors due to weakness of muscles but it eventually resolves. Long-term sequels are uncommon [20, 17, 21].

Diagnosis

The clinical signs of KFD are similar to many other viral/hemorrhagic fevers. Isolation of virus and some antibody based detection methods such as hemagglutination inhibition (HI), complement fixation (CF) and neutralization test (NT) were used [22]. Various molecular diagnostic methods were developed with encroachment of technologies. After establishment of the first BSL-3 laboratory of India at NIV, Pune, real-time RT-PCR, RT-PCR and detection of IgM and IgG antibodies by ELISA were developed and standardized [1]. Virus isolation of KFDV can be done by *in vitro* using BHK-21, Vero E6 cell lines and embryonated chick cell or in mice [23]. KFD anti-IgM antibodies can be detected using ELISA during the acute phase. RT-PCR and real time PCR provides a very rapid and accurate diagnosis [24]. The RT-PCR reactions are highly specific and sensitive compared to other conventional methods [25].

Treatment

There is no specific treatment except supportive and symptomatic ones. Supportive therapy includes the maintenance of normal blood cell counts, blood pressure and hydration [26]. For secondary infections antipyretics, pain reliefs, antimicrobial therapy and blood transfusion are carried out while for nervous disorders, anticonvulsants, and corticosteroids are available [18]. Blood transfusion is done if the situation demands [27]. No particular measures of isolation of patients seem to be indicated [22].

Prevention and Control

Due to the changes taking place in the resistance of acaricide, health policies for the public, environmental changes and development of new pathogen variants, a number of tick-borne diseases are emerging. To reverse them, proper measures are needed to be implemented. Prevention policies including timely diagnosis, quarantine, control of tick and vaccination will act as a constraint to the spread of the virus to other regions. The virus that causes KFD is categorized as a risk group IV pathogen and vaccination has been considered as one of the foremost strategies for the control of KFD [27]. Formalin inactivated tissue culture KFD vaccine is in use since 1990. Initially 2 doses were used in persons of 7–65 years of age, in an interval of 4 weeks. Revaccination is required after 6–9 months for five years [28]. The first series is followed by a booster at 6–9 months and then successive boosters after every 5 years [29]. A likely transmission of infection from a dead monkey to human can be prevented by use of insecticides in about a radius of 50 m circling the dead monkey. However, control programmes are difficult in practice as technically it is not feasible to carry a huge amount of water required for the spray of insecticide. Alternatively, tick-bite can be avoided by using repellents [16].

In order to combat ticks, reduction of the source is also a chief control and preventive measure. Benzene hexachloride (BHC) has been discovered to be one of the most effective chemical. Imparting health education to community will pave the way for the effective control of KFD. Advise people not to go to the forest where monkey deaths are reported. All the local people of villages, wildlife professional photographers, travelers, camp personnel at forest must be counseled to use tick repellents such as NN-Diethyl-m-Tolamide and Dimethyl phthalate [30]. Moreover, to prevent direct contact with ticks, people should be instructed to use clothes having long sleeves [29]. Washing clothes and body with hot water and soap after returning from the forest are other preventive measures to avoid tick infestation [9]. Control, policy formation & strict administrative measures against increased rate of illegal felling of trees and deforestation need to be ensured [22].

Conclusion

The KFDV previously localized within the Shimoga district of Karnataka has gradually spread to the nearby Western Ghats districts in the last few decades. The present review covers various aspects of KFD including epidemiology, mode of transmission, clinical manifestations, diagnosis, treatment and control measures. A long term study on the distribution and abundance of *Haemaphysalis* and other important tick vectors, in respect to the relevant host availability and vegetation biology, are required. In addition, the search for effective anti-viral drugs with successive targets should be a

priority because of the short-lived immunity conferred by the vaccine in use.

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