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Does the rise in cases of Kyasanur forest disease call for the implementation of One Health in India?

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ABSTRACT

The viral hemorrhagic illness known as Kyasanur forest disease (KFD), also referred to as monkey fever, is transmitted by ticks. The etiological agent, which was formerly isolated from monkeys, is Kyasanur forest disease virus (KFDV), an RNA virus belonging to the family Flaviviridae. Since 1957, India has reported 400–500 cases annually, with a case fatality rate of 1–3%. Shiroma, Chikkamagalore, Uttara Kannada, Dakshina Kannada, and Udupi are the five regions in Karnataka, India where KFD is highly prevalent, with around 3263 notified cases reported between 2003 and 2012, of which 823 cases were laboratory confirmed.

The symptoms of monkey fever can range from mild sickness to severe neurological sequelae. Currently, prophylaxis involves administration of formalin-inactivated tissue culture vaccine. Despite the continuing vaccination programs in endemic areas for KFD, new cases are being reported. The current availability and effectiveness of the vaccine are not enough to provide protective immunity and thus prevent new outbreaks.

Our study examined the known literature, knowledge gaps, and host responses associated with KFD. There is a need for robust vector control, public awareness campaigns, mass vaccination programmes, a full understanding of the eco-epidemiological elements of the disease, and implementation of a One Health program. These could all support prevention and management protocols, and thus help to address the issue.

Introduction

Ticks are prevalent and persistent blood-sucking ectoparasites, which serve as vectors for a range of disease-causing organisms, including bacteria, viruses, and protozoans [1]. The main issue with tick bites is that they frequently go untreated, because they are mostly painless and therefore receive minimal medical attention. Ticks are plentiful pathogen reservoirs, infesting areas such as grasslands, fields, forests, and pastures, which consequently become active hotspots for tick-borne disease (TBD) [2]. Human contact and behaviour may raise the risk of transmission, while climatic and environmental factors have a significant influence on tick-borne pathogens. Tick growth and survival are determined by ecological parameters, climatic factors, habitat characteristics, and host–agent–environment interactions, all of which play an important role in tick distribution around the globe [3,4].

The TBD Kyasanur forest disease (KFD), predominantly transmitted by a *Haemophysalis spinigera* bite, was first identified in Kyasanar forest in the Shimoga district of India's Karnataka state in 1957. Kyasanur forest disease virus (KFDV) is in a group of mammalian tickborne viruses of the family Flaviviridae and genus *Flavivirus* [5]. It is potentially pathogenic and can cause hemorrhagic illness in both primate and non-primate animals, such birds, rodents, and squirrels. Kyasanur forest sickness (KFS) has an incubation period of 3–8 days and presents with a variety of symptoms, such as chills, headache (primarily in the frontal region), muscle aches, vomiting, gastrointestinal issues, bleeding problems, and a high fever lasting 5–12 days. The overall mortality rate ranges between 3% and 5% [6].

Despite KFD's widespread incidence in endemic regions, very little is known about its pathogenic processes or the host's reaction to infection. There is some disagreement over its characteristic symptoms, which go beyond an acute febrile sickness [7]. Although hemorrhaging may not always occur, KFD was previously classified as a form of viral hemorrhagic fever. Furthermore, KFDV rarely results in serious neurological illness, unlike pathogens in the tick-borne encephalitis virus (TBEV) serocomplex, which are related to flaviviruses [8]. However, KFDV bears a striking resemblance with the Alkhurma virus in Saudi Arabia and Egypt, which has also been shown by serological investigations and genomic analysis to be a member of a group of mammalian tick-borne viruses linked with hemorrhagic fever [9].

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Since 1957, around 400–500 KFD cases per year have reported in India, primarily in southern areas of the country, but it is now spreading to other parts of India, especially the Western Ghats [1]. Until 2012, KFD was limited to five districts in Karnataka, but has since spread to neighbouring districts and states along the Western Ghats. Sporadic outbreaks of KFD have been now been reported in five states across India, including Karnataka, Tamil Nadu, Kerala, Maharashtra, and Goa [10]. Some 3263 instances had been reported in Karnataka by 2012, of which 823 were laboratory confirmed [11]. KFD has no known treatment, while the vaccines that are now available only target a small portion of the affected regions, and are only partially effective in preventing subsequent epidemics [12].

Transmission of KFD

A tick bite or interaction with an infectious agent, particularly a sick or recently diseased monkey, can result in human transmission. There has been no reported transmission from one person to another. While animals such as cows and goats can contract KFD, their contribution to the disease's spread is minimal. Although animals with a viral load may transmit other ticks and provide blood meals for ticks, KFDV transmission from these animals to humans is uncommon. Furthermore, there is no scientific evidence that the unpasteurized milk of any of these animals is capable of transmitting the disease [13].

Era of vaccination and unprecedented shortcomings

As the disease's etiology was established, suggestions for the development of a vaccine began to flow. Several vaccinations were evaluated for their ability to control the disease, including the attenuated KFDV vaccine made in chick embryo fibroblasts. Among these was a suspension of 5–10% RSSE (Russian spring summer encephalitis) virus after formalin inactivation [14,15]. Studies conducted from 1970 onwards revealed a 59% efficacy of the vaccine following the administration of two doses [16,17]. People aged 7–65 years were administered two doses of the vaccine, spaced 1 month apart, as part of campaigns that were conducted during the tick season, mostly from August to November [18]. Due to the short-lived protection provided by the vaccine, booster doses were advised 6–9 months after the initial immunisation, and again after 5 years from the last known case in the area [19]. This programme was continued in all endemic regions of India, including the Southern and Western Ghats, until October 2022, when the Karnataka Department of Health and Family Welfare reported that vaccine stocks were exhausted [20].

The probability of variations and heterogeneity in the currently prevalent KFDV strain, as opposed to the predominant strain used for vaccine manufacturing, may be grounds for discontinuation. The strain currently affecting humans must be resistant to the previously acquired vaccine. Another issue to consider is the paucity of cold chain maintenance when transporting to remote locations, which would result in diminished potency and inadequate disease protection [21].

Anticipation of the unforeseen

In light of the recent COVID-19 pandemic, we are all well aware that even a minor disease outbreak has the potential to become a fully-fledged pandemic. It is an open secret that there are still dormant reservoirs of bacteria, viruses, and other pathogens that are capable of igniting fresh health crises [22]. Due to the fact that KFDV is spread by ticks, which are widely distributed in ecosystems and cannot be totally eradicated, careful research should focus on reducing the disease's fatality rate and incidence. One more pandemic cannot be tolerated, especially while COVID-19 continues to impact healthcare systems.

Challenges and barriers

(1) Burden estimation: There are significant data gaps for populations at high risk. The burden of KFD is growing over time. To better understand the disease, it is important to study its clinical and epidemiological aspects in greater detail, which requires national-level statistics [23]. The absence of such data is mostly due to unreported cases, which could exist throughout India. The main causes are a lack of attention to medical care and apathy in reporting tick bites and associated symptoms.

(2) Community screening: An absence of widespread sentinel surveillance and screening of people at risk is contributing to the disease burden. Most KFD cases go underreported; therefore, only screening at the community level can provide an actual estimate of the burden of disease, which would be helpful in the creation of focused policies by policymakers and stakeholders aimed at reducing the incidence and complications due to KFD.

(3) Deforestation: Continued deforestation and other unfavourable practices, as well as climatic changes, are major ecological drivers that can lead to the dispersion of deadly pathogens by triggering various complex ecological relationships. Clear links have been found between deforestation and the regions in which current outbreaks of KFD are occurring. The increase in KFDV transmission and spread to new regions can also be attributed to deforestation and the expansion of human habitats into forested areas [7]. As human activity increases in forested areas, it often brings animals directly into contact with humans, who can potentially harbour the ticks. Because of these issues, the prevalence of these deadly infective pathogens has increased at a very fast rate, which could lead us towards an epidemic.

The way forward

(1) Health education and awareness: Despite the government's ongoing efforts and initiatives to reduce the number of new cases in endemic areas, the number of cases continues to rise. Increased awareness of disease occurrence, protective measures, prompt treatment, and examination of livestock for any known symptoms will all contribute to a reduction in cases [24]. The main obstacle lies not only with the availability of effective vaccines, but also their accessibility. The apparent perception of vaccination as painful is one reason why locals frequently resist obtaining an annual booster dose. In addition, the inadequate vaccination coverage for KFD can be attributed to lack of knowledge, the low perceived risk, geographical challenges, and accessibility issues, particularly in remote locations. Therefore, effective solutions, such as ensuring an adequate vaccine supply and implementing thorough local planning are essential [25].

(2) Safe and sustainable diagnostics for detecting infected human subjects and vectors for routine surveillance: In India, safer assays could be useful in the disease hotspots for routine KFD monitoring among vectors and humans. Innovative methods, using chemically synthesised virus-based diagnostic tests as well as Truenat KFD (a real-time polymerase chain reaction-based assay), should be introduced for the detection of KFDV in remote and inaccessible areas [26]. Increased accessibility of screening tests will aid in tracing the magnitude of pathogen distribution and diversification, if any, through large-scale surveillance across the country. This will help in identifying not only diseased humans, but also diseased animals. Moreover, improving scientific and clinical tools — for assessing and enhancing the effectiveness of treating KFD symptoms — should be associated with establishing operational guidelines for their application.

To better track the spread of KFD, it is advised to implement fever case and serological surveys in regions beyond the current known range of KFD in order to predict spillovers [27]. Using tick surveillance, which has proven to be effective in predicting spillovers in similar systems, can aid in monitoring the persistence of KFDV transmission over time [28]. Monkey surveillance is currently being conducted by passively monitoring deceased or ill monkeys, but is limited to regions where resources and awareness of KFD are sufficient [24].

(3) Robust strategies for vector control: Controlling the spread of disease can be greatly aided by the identification of hotspots, cross-border consultation with veterinarians, early detection of new cases, studies of local residents' behaviour, and timely medical assistance for those who may have been bitten by ticks. Increased vigilance among frontline or healthcare workers would help to track the vector population. This can be achieved by in-depth entomological research, climate investigations, and topographic analysis. Pesticides can be used as a preventive or control measure.

(4) Dual immunization: The vaccination of suspected monkey cases can aid in reducing the spread of cases, in the same way that humans are immunised as a part of ongoing control measures. Radio-tracking of wildlife and primate immunisation, particularly with ingestible vaccines, have the potential to stop the spread of diseases from monkeys to people. The idea of creating an edible vaccine for controlling KFD is a promising long-term strategy, with the potential to benefit both primates and non-primates, although the development process may take over a decade [29]. The impact of the proposed vaccination of non-human primates would support the country's continuing preventive and control efforts against KFD.

(5) Implementation of a One Health (OH) approach for the prevention and control of KFD: Because of the intricate transmissive cycle of the disease, a transdisciplinary strategy and multisectorial engagement across individuals and organizations involved in the community, livestock, and environmental health domains are preferable for preventing KFD transmission [30]. The OH project is extensive and cross-sectoral, although the non-scientific community has little involvement, because of an apparent a lack of knowledge exchange and development of new concepts. Some recommendations are as follows:

(a) Broaden the stakeholder structure to include non-governmental entities, such as hospitals and community leaders.

(b) Implement cooperative initiatives, such as campaigns for community- and sector-specific perspectives.

(c) Improve campaigns by including social and mainstream media, and thus expanding the range of viewpoints regarding KFD.

(d) Improve processes for co-steering, communication, observation, data storing, and data sharing. In addition to increasing the approach's transparency, recognition, and interchange with other surveillance initiatives outside of the region, such processes would also make it easier to formally assess the approach's accomplishments and weaknesses and, if necessary, to revise and improve it.

(e) It is necessary to diversify the knowledge foundations on which surveillance and control are built, to increase their authenticity and cultural relevance to the affected people, and also to facilitate their reform and adaptability via specialized methods for integrating the knowledge gained.

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Ethical approval statement

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Conflicts of interest

None declared.

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