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Why has an Optimally Effective Vaccine for Kyasanur Forest Disease has not yet been achieved? A Scientific, Biological, Immunological, Ecological, and Community-Level Perspective

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Abstract

The Kyasanur forest disease (KFD) is a tick-borne disease that is endemic to Western Ghats in India. There is a formalin-inactivated vaccine for KFD virus, but it has been difficult to find one that is consistently effective or durable. Many scientific and translational factors contribute to this problem. First, the cycle of zoonotic transmission is quite complex. Second, human exposure happens episodically. Third, there is considerable genetic variation among the circulating strains of the virus. Additionally, flavivirus-specific immunological challenges such as the requirement for balanced humoral and cellular immunity and the risks of antibody-dependent enhancement make the use of traditional vaccination platforms difficult. KAP (knowledge-attitude-practice) studies indicate that variability in vaccine acceptance and community awareness of vaccine use and booster schedules seem to be significant factors affecting real-life efficacy of vaccines. Thus, the lack of an optimally effective KFD vaccine is due to multiple facets of the complexity of KFD, rather than lack of effort. Reverse vaccinology, immuno-informatics, and community-engaged vaccine development approaches are promising avenues for developing next-generation KFD vaccines and represent the best path for long-term, sustainable control of KFD in today's world.

Keywords: *Kyasanur Forest Disease, Vaccine, KAP, Zoonotic infection.*

Introduction

Kyasanur Forest Disease (KFD) is a tick-borne viral hemorrhagic fever first identified in 1957 in the Kyasanur Forest of Karnataka, India [1]. The causative agent, Kyasanur Forest Disease Virus (KFDV), belongs to the genus Flavivirus within the family Flaviviridae and is closely related to other medically important flaviviruses such as tick-borne encephalitis virus (TBEV) and Omsk hemorrhagic fever virus (OHFV) [2], [3]. It is one of the earliest diagnosed tick-borne viral hemorrhagic fevers in India and remains a geographically limited expanding zoonosis. Since it was first identified in the late 1950s, KFD continues to pose a threat to public health as KFD is recurrent public health problem, especially among populations that live near forests and are in occupations that expose them to KFD. The disease has the following characteristics: (1) acute febrile illness; (2) hemorrhagic symptoms; and (3) occasional neurological symptoms; therefore, KFD causes significant morbidity among people living in endemic areas [4], [5], [6].

Geographic Distribution and Expansion

KFD was initially restricted to the Shimoga district of Karnataka, India, but has demonstrated significant geographic expansion over the past six decades [6], [7]. The disease has now been reported in at least 14 districts across Karnataka, including Uttara Kannada, Udupi, Chikkamagaluru, and Dakshina Kannada, with sporadic cases and serological evidence extending into Gujarat, Rajasthan, West Bengal and neighboring states like Kerala, Tamil Nadu, and Goa [8], [9], [10] (Figure:1). The expansion of KFD along the Western Ghats demonstrates that KFD is an ecologically dynamic disease. The expansion of KFD has followed predominantly through forested areas of the Western Ghats where ecological conditions are conducive to the continued survival of tick vectors and vertebrate reservoir hosts [11], [12]. In Karnataka, the disease burden associated with KFD continues to be highest, with repeated outbreaks reported in the districts of Shivamogga, Uttara Kannada, Chikkamagaluru, and Dakshina Kannada.

In Kerala, districts bordering Karnataka (i.e., Wayanad and Malappuram) have reported cases, and there are sporadic outbreaks and evidence of seropositive animals and/or humans indicating continued silent transmission of KFDV in Goa and Maharashtra [10]. Reports from Tamil Nadu, especially from forested regions of the Nilgiris and adjoining districts, further underscore the southward expansion of the virus. Historically confined to limited forested zones, KFD has demonstrated progressive spatial expansion over the past six decades [6], [7]. Surveillance data indicate annual case counts ranging between 400 and 600 in endemic regions, although under-reporting remains a concern due to limited diagnostic access in remote forest-fringe communities[11], [13], [14]. Transmission exhibits strong seasonality, peaking between November and June when tick activity is highest [2], [15]. Environmental drivers of this expansion include deforestation, land-use changes, climate-mediated alterations in tick ecology, increased human–wildlife interaction, and livestock movement [16], [17]. Migratory birds may also contribute to long-distance dispersal of infected ticks, facilitating the establishment of new endemic foci [18], [19].

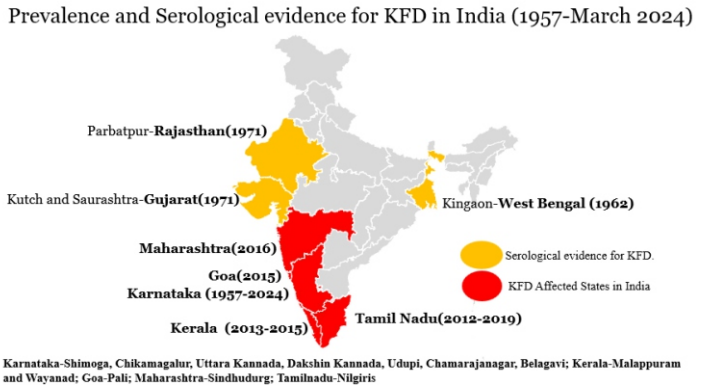

Figure 1: Indian map showing the prevalence of KFD across the Western Ghats and the States with Serological evidence for KFDV

The ecological and anthropogenic factors related to the expansion of KFD include deforestation, land use changes, increased human intrusion into forest ecosystems, livestock movement, and changes to tick/host interactions. For years, efforts to control KFD have been thwarted by the difficulty of obtaining effective antiviral treatments for KFD. Furthermore, most existing vaccines provide only short-term protection in populations that have had little or no prior exposure, creating increased risk of KFD outbreaks and increased morbidity from KFD infections.

Ecological Complexity and Zoonotic Transmission

A fundamental challenge in controlling KFD is due to the complexity of its zoonotic transmission cycle. The primary vectors are ixodid ticks, with *Haemaphysalis spinigera* serving as the principal vector, though other species including *H. turturis, H. kyasanurensis, and H. minuta* have also been implicated [20], [21]. These ticks exhibit transstadial and transovarial transmission, allowing viral persistence in tick populations across seasons [22]. KFDV is transmitted among *Haemaphysalis* ixodid ticks and several species of small mammals, including multiple non-human primate species; humans are considered incidental hosts; therefore, humans are not responsible for the prolonged transmission of KFDV, eliminating the opportunity to achieve herd immunity or interrupt KFDV transmission by merely implementing human-oriented intervention strategies [5], [23]. The enzootic cycle involves various wildlife species, with langurs (Semnopithecus entellus) and bonnet macaques (Macaca radiata) serving as amplifying hosts [20], [21], [24]. Other mammals, including shrews, squirrels, and various bird species, contribute to viral maintenance and dispersal [2]. Humans are considered dead-end hosts, as viremia levels are typically insufficient to infect feeding ticks [25]. Ecological studies have identified specific habitat requirements for KFDV transmission, including deciduous and semi-evergreen forests with dense undergrowth that support tick populations [[6], [24]. Microclimate factors such as humidity, temperature, and vegetation density significantly influence tick survival and viral persistence [26], [27]. The episodic nature of KFD outbreaks (seasonal) along with the absence of symptomatic KFD cases during silent viral circulation within forest ecosystems, also creates significant limitations for surveillance systems and the development of reliable immune correlates of protection.

Clinical Manifestations and Pathogenesis

KFD presents as an acute febrile illness with a typical incubation period of 3-8 days following tick bite [28], [29]. The disease typically manifests in two phases: an initial febrile phase lasting 3-5 days, characterized by sudden onset of high fever, severe headache, myalgia, and prostration [6], [30]. This may be followed by a brief afebrile period, after which some patients develop a second phase with neurological complications or hemorrhagic manifestations [31]. Hemorrhagic symptoms, occurring in approximately 10-15% of cases, include epistaxis, hematemesis, melena, and petechial rashes [15], [28]. Neurological complications, observed in 10-20% of patients, range from altered consciousness and seizures to meningoencephalitis and focal neurological deficits[7]. Laboratory findings typically include thrombocytopenia, leukopenia, and elevated liver enzymes [6], [29], [32]. The pathogenesis of KFD involves viral replication in reticuloendothelial tissues, leading to viremia and systemic dissemination[25], [33]. Histopathological studies reveal hemorrhagic necrosis in various organs, including liver, kidneys, lungs, and brain, with prominent involvement of the reticuloendothelial system[34]. The immune response involves both innate and adaptive components, with cytokine dysregulation contributing to disease severity [5].

Immunological Issues in Developing Vaccines for KFD

The flavivirus family includes KFDV, which has its own unique set of immunological challenges. To achieve a protective immune response, there is a need for optimal levels of neutralizing antibodies and strong cell mediated (T cell) immunity, each of which contribute separately to the overall response against virus infection. Although neutralizing antibodies constitute a critical component of the immune response in flaviviruses as documented by research [35], [36], flavivirus infections have also been associated with antibody-dependent enhancement (ADE), where sub-neutralising levels of antibodies can lead to enhanced disease severity upon subsequent infection [37], [38]. The limited immunological studies in humans with KFD, inability to do human challenge studies, and a lack of knowledge relating to the durability of the long term memory immune response have hindered the rational development of vaccines to KFD. These three limitations create challenges in selecting the appropriate antigens to include in a KFD vaccine and achieving durable cross-protective immunity.

Limitations of the Currently Available Formalin Inactivated Vaccines

The currently used chick embryo fibroblast (CEF)–derived, formalin-inactivated KFD vaccine has been deployed for over five decades [39], which were available and appropriate at the time of introduction.

The vaccine has been successfully utilised for mitigating disease in endemic KFD areas; however, a number of evaluations of the vaccine in the field have shown that the vaccine elicits waning immunity, has a need for multiple booster doses and variable effectiveness against the vaccine virus in a real world setting [40], [41]. Efficacy studies have shown variable protection rates, ranging from 62-82% depending on the study population and methodology [40]. The vaccine requires a primary series of two doses given one month apart, followed by annual boosters to maintain immunity [42]. Field effectiveness studies have indicated waning immunity over time, necessitating regular revaccination campaigns [40]. Studies have shown that inactivated vaccines induce less robust T-cell responses compared with live-attenuated or recombinant viral vaccines[43]; therefore, it is expected and has been documented that protective antibody titre declines due to time, particularly for populations that experience repeated exposures (e.g. seasons of exposure) or have not received adequate amounts of the vaccine (e.g. those who have never or infrequently received the vaccine). These factors do not suggest that the existing CEF vaccine has insufficient efficacy against KFD; however, the efficacy of the CEF vaccine may be further enhanced through improvements to the existing CEF vaccine or new vaccines for KFD.

Viral Genetic Variability and Geographical Spread

Although KFDV has been regarded as largely stable from a genetic perspective, numerous studies show that the virus exhibits regional variation as it continues to expand into new ecological niches along the Western Ghats [44], [45]. Even minor differences in the amino acids of viral proteins that dominate immune responses can influence how vaccinated individuals recognize epitopes on that protein, thus limiting the degree of cross-protection afforded by vaccines [44], [46]. The on-going evolution of KFDV is a reason to develop immunization strategies that will focus on dominant epitopes that are conserved among circulating KFDV strains and therefore will be able to provide broad, durable protection.

Manufacturing and Supply Chain Challenges

India's KFD vaccination programme has repeatedly encountered multiple supply chain constraints and manufacturing delays that limit its success. Programmatic report data and field-level evaluations collected from endemic districts demonstrate that during periods when the disease is being transmitted (transmission season) vaccine availability has been intermittent; vaccine vial shipping from the manufacturer to the peripheral delivery facility has been delayed (sometimes with vials arriving at the last facility near the expiration date); and the cold chain has been disrupted in remote forest periphery areas due to unreliable electricity and last mile logistics. These issues have prevented the vaccination programme from being completed in a timely manner (by completing all doses in the series) and have reduced overall vaccinations completed [47], [48]. Additional operational guidance provided by Karnataka indicates there was a need for regular district-level supply planning/indents and logistics coordination to minimise the impact of stock-outs on KFD vaccination programmes, suggesting that the overall KFD vaccination programme has been built upon systemic reliance upon unfettered procurement and distribution paths [49]. The inability to complete KFD vaccination schedules in a timely manner creates low vaccination coverage and substantial drop-out between doses and/or boosters, which have been documented in community-based operational research from endemic areas in western India [42].

Community-Level Determinants and KAP Evidence

The increasing geographical reach of KFDV has serious implications for controlling the disease. It requires a robust surveillance system, as well as coordination of responses across state borders, and highlights the need for disease prevention strategies (improved vaccines that provide broad protection) that can be implemented on a regional basis. The continued expansion of KFDV throughout multiple states will reinforce the argument for implementing comprehensive, preventive, and vaccine-based approaches to control the disease rather than relying solely on localized interventions [50]. In addition to biological limitations, there are also important community-level factors affecting the ability to control KFD in the community setting. In endemic regions, KAP studies show significant variability in KFD awareness, acceptance of vaccination, and adherence to booster shots [40], [51]. Myths and misunderstandings about the virus and KFD have also affected the uptake of vaccines. The belief that vaccines are not safe, concern about side effects, and job-related barriers for forest workers as well as challenges associated with accessing vaccination services play a significant role in the uptake of vaccines. In addition, most field trials of vaccine efficacy are composite measures of biological efficacy and human behaviour, not immunogenicity alone [52]. In the absence of curative therapies, the majority of individuals consider vaccination to be the best preventive measure, and therefore it is essential for vaccine design and delivery strategies to meet the needs of the community[53].

Current Preventive and Control Strategies

Currently there are no approved anti-viral therapies to treat KFD, and the only way to manage patients is through supportive care and symptomatic relief[54]. This includes providing adequate hydration, managing bleeding and keeping a watchful eye for the onset of neurological symptoms [1], [4], [23]. While supportive care can reduce mortality rates if administered in a timely fashion, it does not reduce the amount of virus produced in the body and do not change the progression of the disease [55]. The feasibility of implementing Therapeutic-Based Control Strategies for KFD has many limitations. KFD generally has an acute onset of symptoms and typically has rapid widespread dissemination throughout the body. The onset and dissemination of this disease frequently occurs in remote forest edge areas, where diagnosis is delayed and access to medical services can be impossible. With these constraints, the therapeutic window for intervention with an anti-viral therapy is drastically shortened [56]. Although broad-spectrum antivirals and flavivirus specific medicines have been studied for use with KFD patient the clinical effectiveness has yet to be proven and no clinical protocols have been established through the use of these types of medications as treatment options [38]. The absence of effective treatments for KFD ultimately supports the case for pursuing next-generation vaccine research as a priority versus de-emphasizing next-generation vaccine research for KFD. By providing protection from the onset of illness, preventive vaccines can address delays in diagnosis and healthcare that negatively impact treatment success. Advances in reverse-vaccinology, immunoinformatics and epitop-based vaccine design enable identification of conserved antigenic sites, prediction of extensive HLA coverage, and optimization of immune response while minimizing the risk of ADE [57], [58]. Further compounding these challenges, periodic interruptions and temporary suspension of KFD vaccination in Karnataka have occurred in recent years, largely due to concerns related to vaccine quality assurance, batch potency, and safety evaluations.

Such interruptions, while necessary from a regulatory and public-health safety perspective, have resulted in missed vaccination windows during peak transmission seasons and have disrupted continuity of booster dosing in already vulnerable populations [40], [53], [59], [60]. These episodic halts reinforce the fragility of the current KFD vaccine supply ecosystem and highlight the need for more robust, scalable, and quality-assured manufacturing systems to ensure uninterrupted protection in endemic areas.

Integrated Control Framework for KFD

Control of Kyasanur Forest Disease (KFD) can be accomplished through an integrated system of control, with an emphasis on prevention, and using the following techniques:

- Efficiently designing vaccines using precision vaccinology.
- Communities to develop interventions based on knowledge, attitude, and practice (KAP) studies.
- Improved surveillance systems and ecological awareness.
- Clinician support of patients should occur, even in the absence of treatment.

This approach reflects the understanding that no single intervention will suffice; therefore, sustainable control can only be achieved by combining biological innovation with socio-ecological realities.

Conclusion

In my opinion, the path to the best vaccine for Kyasanur Forest Disease is limited by the complexity of the disease and not by a lack of effort to develop one. Over the last few decades, both public health and government entities have been consistently and genuinely working towards controlling KFD by implementing vaccination campaigns, surveillance programs, and responding to outbreaks of the virus. However, as KFD continues to evolve geographically and biologically, new solutions to prevent and control KFD must also continually evolve. Expansion poses challenges to both existing surveillance systems and interstate coordination; additionally, the urgency for developing preventive/educational strategies, including effective vaccines that will protect against many circulating KFD viruses, is emphasized. A multifaceted strategy that incorporates both scientific advances from immunoinformatic research and novel approaches to vaccine design, combined with greater community involvement are required for making a significant impact on controlling KFD. Creating new ways to combat KFD should not be viewed as creating shortcomings of existing methods; we should see creating new solutions to KFD as opportunities to develop better strategies for creating new methods, refining existing processes, and ultimately achieving sustainable and effective control of KFD.

The fact that neither an effective vaccine nor a specific therapy exists for KFD highlights the extent of multiple dimensions of complexity associated with the disease (e.g., ecological uncertainty related to KFD occurrence, flavivirus immunology, virus diversity, and community-level factors). This review does not suggest that research is lacking; rather, it underscores the need for integrated research efforts employing next-generation approaches. Currently, the scientific rationale for developing safer, more effective and appropriate KFD vaccines is strong due to the ongoing integration of KAP studies, reverse vaccinology, and next-generation vaccine platforms. The public health burden associated with Kyasanur Forest Disease will be reduced in rural localized regions in endemic areas through the successful development of KFD vaccines.

Abbreviations

KFD-Kyasanur Forest Disease
KFDV – Kyasanur Forest Disease Virus
CEF – Chick Embryo Fibroblast
ADE- Antibody Dependent Enhancement
KAP- Knowledge, Attitude and Practice study
HLA-Human Leukocyte Antigen

Disclosure of interest

The authors declare that they have no competing interest.

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References

1. M. R. Holbrook, "Kyasanur forest disease," Dec. 2012. doi: 10.1016/j.antiviral.2012.10.005. *Antiviral Research*.
2. M. V Murhekar, G. S. Kasabi, S. M. Mehendale, D. T. Mourya, P. D. Yadav, and B. V Tandale, "On the transmission pattern of Kyasanur Forest disease (KFD) in India.," *Infect. Dis. Poverty*, vol. 4, p. 37, Aug. 2015, doi: 10.1186/s40249-015-0066-9.
3. K. A. Dodd et al., "Ancient Ancestry of KFDV and AHFV Revealed by Complete Genome Analyses of Viruses Isolated from Ticks and Mammalian Hosts," *PLoS Negl. Trop. Dis.*, vol. 5, no. 10, p. e1352, Oct. 2011, doi: 10.1371/journal.pntd.0001352.
4. P. Pattnaik, "Kyasanur forest disease: An epidemiological view in India," *Rev. Med. Virol.*, vol. 16, no. 3, pp. 151–165, 2006, doi: 10.1002/rmv.495.
5. B. Sawatsky, A. J. McAuley, M. R. Holbrook, and D. A. Bente, "Comparative pathogenesis of Alkhumra hemorrhagic fever and Kyasanur forest disease viruses in a mouse model.," *PLoS Negl. Trop. Dis.*, vol. 8, no. 6, p. e2934, Jun. 2014, doi: 10.1371/journal.pntd.0002934.
6. K. Pavri, "Clinical, Clinicopathologic, and Hematologic Features of Kyasanur Forest Disease," *Clinical Infectious Diseases*, vol. 11, no. Supplement_4, pp. S854–S859, May 1989, doi: 10.1093/clinids/11.Supplement_4.S854.
7. T. H. Work, F. R. Roderiguez, and P. N. Bhatt, "Virological Epidemiology of the 1958 Epidemic of Kyasanur Forest Disease," *Am. J. Public Health Nations Health*, vol. 49, no. 7, p. 869, 1959, doi: 10.2105/AJPH.49.7.869.
8. C. Sadanandane, A. Elango, N. Marja, P. V Sasidharan, K. H. K. Raju, and P. Jambulingam, "An outbreak of Kyasanur forest disease in the Wayanad and Malappuram districts of Kerala, India.," *Ticks Tick. Borne. Dis.*, vol. 8, no. 1, pp. 25–30, 2017, doi: 10.1016/j.ttbdis.2016.09.010.
9. S. K. Kiran et al., "Kyasanur Forest disease outbreak and vaccination strategy,Shimoga District, India, 2013-2014," *Emerg. Infect. Dis.*, vol. 21, no. 1, pp. 146–149, Jan. 2015, doi: 10.3201/eid2101.141227.
10. D. Y. Patil et al., "Occupational exposure of cashew nut workers to Kyasanur Forest disease in Goa, India," *International Journal of Infectious Diseases*, vol. 61, pp. 67–69, Aug. 2017, doi: 10.1016/J.IJID.2017.06.004.
11. D. T. Mourya and P. D. Yadav, "Recent Scenario of Emergence of Kyasanur Forest Disease in India and Public Health Importance," Mar. 01, 2016, *Springer Verlag*. doi: 10.1007/s40475-016-0067-1.
12. S. Ghosh, P. Azhahianambi, and M. P. Yadav, "Upcoming and future strategies of tick control: a review.," *J. Vector Borne Dis.*, vol. 44, no. 2, pp. 79–89, Jun. 2007.
13. D. T. Mourya et al., "Spread of Kyasanur Forest disease, Bandipur Tiger Reserve, India, 2012-2013," *Emerg. Infect. Dis.*, vol. 19, no. 9, pp. 1540–1541, Sep. 2013, doi: 10.3201/eid1909.121884.
14. A. Munivenkatappa, R. Sahay, P. Yadav, R. Viswanathan, and D. Mourya, "Clinical & epidemiological significance of Kyasanur forest disease," *Indian Journal of Medical Research*, vol. 148, no. 2, p. 145, 2018, doi: 10.4103/ijmr.IJMR_688_17.
15. M. G. Varma, H. E. Webb, and K. M. Pavri, "Studies on the transmission of Kyasanur Forest disease virus by *Haemaphysalis spinigera* Newman.," *Trans. R. Soc. Trop. Med. Hyg.*, vol. 54, pp. 509–16, Nov. 1960, doi: 10.1016/0035-9203(60)90024-9.
16. S. E. Randolph, "Transmission of tick-borne pathogens between co-feeding ticks: Milan Labuda's enduring paradigm.," *Ticks Tick. Borne. Dis.*, vol. 2, no. 4, pp. 179–82, Dec. 2011, doi: 10.1016/j.ttbdis.2011.07.004.
17. F. A. Asaaga et al., "The role of social vulnerability in improving interventions for neglected zoonotic diseases: The example of Kyasanur Forest Disease in India," *PLOS Global Public Health*, vol. 3, no. 2, p. e0000758, Feb. 2023, doi: 10.1371/journal.pgph.0000758.
18. H. Hoogstraal, M. A. Traylor, S. Gaber, G. Malakatis, Ezzat Guindy, and I. Helmy, "Ticks (*Ixodidae*) on Migrating Birds in Egypt, Spring and Fall 1962*," 1964.

19. R. Dhaka, R. Verma, R. Kumar, M. Dhankar, K. Bhalla, and G. Agrawal, "Kyasanur forest disease: a rare viral hemorrhagic disease in India," *Int. J. Community Med. Public Health*, vol. 5, no. 8, p. 3149, Jul. 2018, doi: 10.18203/2394-6040.ijcmph20183042.
20. M. A. Sreenivasan, R. Bhat, and P. K. Rajagopalan, "The epizootics of kyasanur forest disease in wild monkeys during 1964 to 1973," *Trans. R. Soc. Trop. Med. Hyg.*, vol. 80, no. 5, pp. 810–814, 1986, doi: 10.1016/0035-9203(86)90390-1.
21. M. K. Goverdhan et al., "Epizootiology of Kyasanur Forest Disease in wild monkeys of Shimoga district, Mysore State (1957-1964).," *Indian J. Med. Res.*, vol. 62, no. 4, pp. 497–510, Apr. 1974.
22. S. J. Burthe et al., "First evidence of transovarial transmission of Kyasanur Forest disease virus in *Haemaphysalis* and *Rhipicephalus* ticks in the wild," *Parasites and Vectors*, vol. 18, no. 1, Dec. 2025, doi: 10.1186/s13071-024-06643-5.
23. S. Pattnaik, R. Agrawal, J. Murmu, S. Kanungo, and S. Pati, "Does the rise in cases of Kyasanur forest disease call for the implementation of One Health in India?," Jun. 01, 2023, *Elsevier Ltd.* doi: 10.1016/j.ijregi.2023.02.003.
24. P. N. Bhatt, T. H. Work, M. G. Varma, H. Trapido, D. P. Murthy, and F. M. Rodrigues, "Kyasanur forest diseases. IV. Isolation of Kyasanur forest disease virus from infected humans and monkeys of Shimogadistrict, Mysore state.," *Indian J. Med. Sci.*, vol. 20, no. 5, pp. 316–20, May 1966.
25. S. Z. Shah et al., "Epidemiology, Pathogenesis, and Control of a Tick-Borne Disease- Kyasanur Forest Disease: Current Status and Future Directions," *Front. Cell. Infect. Microbiol.*, vol. 8, p. 149, May 2018, doi: 10.3389/fcimb.2018.00149.
26. G Geevarghese and A C Mishra, *Haemaphysalis* Ticks of India, 1st ed. *Elsevier*, 2011. doi: 10.1016/C2010-0-68435-5.
27. R. Balasubramanian, P. Yadav, S. Sahina, and V. Nadh, "The species distribution of ticks & the prevalence of Kyasanur forest disease virus in questing nymphal ticks from Western Ghats of Kerala, South India," *Indian Journal of Medical Research*, vol. 154, no. 5, pp. 743–749, Nov. 2021, doi: 10.4103/ijmr.IJMR_234_19.
28. Work T H, Trapido H, Murthy D P N, Rao R L, Bhatt P N, and Kulkarni K G, "Kyasanur forest disease. III. A preliminary report on the nature of the infection and clinical manifestations in human beings.," *Indian J. Med. Sci.*, vol. 11, no. 8, pp. 619–45, Aug. 1957.
29. M. R. Adhikari Prabha, M. G. Prabhu, C. V Raghuveer, M. Bai, and M. A. Mala, "Clinical study of 100 cases of Kyasanur Forest disease with clinicopathological correlation.," *Indian J. Med. Sci.*, vol. 47, no. 5, pp. 124–30, May 1993.
30. S. Upadhyaya, D. P. Murthy, and C. R. Anderson, "Kyasanur Forest disease in the human population of Shimoga district, Mysore State, 1959-1966.," *Indian J. Med. Res.*, vol. 63, no. 11, pp. 1556–63, Nov. 1975.
31. J. Wang et al., "Isolation of kyasanur forest disease virus from febrile patient, Yunnan, China," *Emerg. Infect. Dis.*, vol. 15, no. 2, pp. 326–328, Feb. 2009, doi: 10.3201/eid1502.080979.
32. Webb H E and Chaterjea J B, "Clinico-pathological observations on monkeys infected with Kyasanur Forest disease virus, with special reference to the haemopoietic system.," *Br. J. Haematol.*, vol. 8, pp. 401–13, Oct. 1962, doi: 10.1111/j.1365-2141.1962.tb06544.x.
33. H. E. Webb, G. Wetherley-Mein, C. E. Gordon Smith, and D. McMahon, "Leukaemia and Neoplastic Processes Treated with Langat and Kyasanur Forest Disease Viruses: A Clinical and Laboratory Study of 28 Patients," *Br. Med. J.*, vol. 1, no. 5482, pp. 258–266, Jan. 1966, doi: 10.1136/bmj.1.5482.258.
34. B. Bhatia, H. Feldmann, and A. Marzi, "Kyasanur Forest Disease and Alkhurma Hemorrhagic Fever Virus-Two Neglected Zoonotic Pathogens.," *Microorganisms*, vol. 8, no. 9, pp. 1–17, Sep. 2020, doi: 10.3390/microorganisms8091406.
35. E. Mehlhop and M. S. Diamond, "Mechanisms of Complement Regulation of Infection by Flaviviruses," in West Nile Encephalitis Virus Infection, New York, NY: *Springer New York*, 2009, pp. 189–217. doi: 10.1007/978-0-387-79840-0_9.
36. B. S. Pillai, S. Jagannathan, S. Jagadibabu, C. S. Kukkaler, and S. Sakthivel, "Immunodominant Protein of Kyasanur Forest Disease Virus: A retrospective study," *Res. J. Biotechnol.*, vol. 19, no. 9, pp. 132–142, Jul. 2024, doi: 10.25303/1909rjbt1320142.
37. S. B. Halstead and S. Zompi, "Protective immune responses to dengue virus infection and vaccines: Perspectives from the field to the bench," 2015, *Frontiers Research Foundation*. doi: 10.3389/fimmu.2015.00075.
38. L. Goo et al., "A protective human monoclonal antibody targeting the West Nile virus E protein preferentially recognizes mature virions.," *Nat. Microbiol.*, vol. 4, no. 1, pp. 71–77, 2019, doi: 10.1038/s41564-018-0283-7.
39. K. V Shah, S. P. Aniker, D. P. Murthy, F. M. Rodrigues, M. S. Jayadeviah, and H. A. Prasanna, "Evaluation of the field experience with formalin-inactivated mouse brain vaccine of Russian spring-summer encephalitis virus against Kyasanur Forest disease.," *Indian J. Med. Res.*, vol. 50, pp. 162–74, Mar. 1962.
40. G. S. Kasabi et al., "Coverage and Effectiveness of Kyasanur Forest Disease (KFD) Vaccine in Karnataka, South India, 2005-10," *PLoS Negl. Trop. Dis.*, vol. 7, no. 1, p. e2025, 2013, doi: 10.1371/journal.pntd.0002025.
41. R. Khandia et al., "Modulation of Dengue/Zika Virus Pathogenicity by Antibody-Dependent Enhancement and Strategies to Protect Against Enhancement in Zika Virus Infection.," *Front. Immunol.*, vol. 9, p. 597, 2018, doi: 10.3389/fimmu.2018.00597.
42. A. Oliveira Id, K. Selvaraj, J. P. Tripathy, U. Betodkar, J. Cacodcar, and A. Wadkar, "Kyasanur Forest Disease vaccination coverage and its perceived barriers in Goa, India-A mixed methods operational research," 2019, doi: 10.1371/journal.pone.0226141. *PLoS ONE*.
43. N. K. Pariyapurath et al., "Cocktail Antigen Presenting Peptide Vaccine Development for Nipah Virus: An Immunoinformatic Approach to Indian and Malaysian Strain," *J. Pure Appl. Microbiol.*, 2025, doi: 10.22207/JPAM.19.3.54.
44. R. Mehla et al., "Recent ancestry of Kyasanur Forest disease virus," *Emerg. Infect. Dis.*, vol. 15, no. 9, pp. 1431–1437, Sep. 2009, doi: 10.3201/eid1509.080759.
45. D. T. Mourya et al., "Diagnosis of Kyasanur forest disease by nested RT-PCR, real-time RT-PCR and IgM capture ELISA," *J. Virol. Methods*, vol. 186, no. 1–2, pp. 49–54, Dec. 2012, doi: 10.1016/J.JVIROMET.2012.07.019.
46. P. Yadav et al., "Kinetics of viral RNA, immunoglobulin-M & G antibodies in Kyasanur forest disease," *Indian Journal of Medical Research*, vol. 150, no. 2, pp. 186–193, Aug. 2019, doi: 10.4103/ijmr.IJMR_1929_17.
47. S. K. Vedachalam et al., "Kyasanur Forest Disease: An Epidemiological Investigation and Case-Control Study in Shivamogga, Karnataka, India-2022," *Int. J. Public Health*, vol. 69, 2024, doi: 10.3389/ijph.2024.1606715.
48. S. K. Kiran et al., "Kyasanur Forest disease outbreak and vaccination strategy,Shimoga District, India, 2013-2014.," *Emerg. Infect. Dis.*, vol. 21, no. 1, pp. 146–9, Jan. 2015, doi: 10.3201/eid2101.141227.
49. "Operational Manual: Kyasanur Forest Disease(2020)".
50. S. Sidhik, S. Santhosh, and B. Rathinam, "Knowledge, Attitudes, and Practices Regarding Ticks, Tick-Borne Diseases, and Ethnomedicine Among an at-Risk Population in Kerala," *Vector-Borne and Zoonotic Diseases*, vol. 24, no. 2, pp. 86–94, Feb. 2024, doi: 10.1089/vbz.2023.0040.
51. G. S. Kasabi et al., "Kyasanur Forest disease, India, 2011-2012.," *Emerg. Infect. Dis.*, vol. 19, no. 2, pp. 278–281, 2013, doi: 10.3201/eid1902.120544.
52. J. McLenon and M. A. M. Rogers, "The fear of needles: A systematic review and meta-analysis," *J. Adv. Nurs.*, vol. 75, no. 1, pp. 30–42, Jan. 2019, doi: 10.1111/jan.13818.
53. S. B. Pillai et al., "Advancements in Vaccine Development: A Comprehensive Design of a Multi-Epitopic Immunodominant Peptide Vaccine Targeting Kyasanur Forest Disease via Reverse Vaccinology," *Open Biotechnol. J.*, vol. 20, 2026, doi: 10.2174/0118740707423079251207205822.
54. S. B. Pillai et al., "Monkeypox and Monkey Fever: Basic Understanding for Better Community Participation in Disease Control," *Biotechnology Journal International*, vol. 26, no. 5, pp. 1–12, Oct. 2022, doi: 10.9734/bji/2022/v26i5657.
55. N. K. Pariyapurath et al., "Targeted Immunization Strategies and Designing Vaccine against Indian Nipah Virus Strain (NiV B) and Malaysian Variant (NiV M)," Original Article *International Journal of Pharmaceutical Investigation*, vol. 14, no. 4, pp. 1201–1207, 2024, doi: 10.5530/ijpi.14.4.131.
56. P. D. Yadav et al., "Outbreak of Kyasanur Forest disease in Thirthahalli, Karnataka, India, 2014," *International Journal of Infectious Diseases*, vol. 26, pp. 132–134, 2014, doi: 10.1016/j.ijid.2014.05.013.
57. R. Rappuoli, M. J. Bottomley, U. D'Oro, O. Finco, and E. De Gregorio, "Reverse vaccinology 2.0: Human immunology instructs vaccine antigen design," *Journal of Experimental Medicine*, vol. 213, no. 4, pp. 469–481, Apr. 2016, doi: 10.1084/JEM.20151960.
58. T. Cohen, L. Moise, W. Martin, and A. S. De Groot, "Immunoinformatics: The Next Step in Vaccine Design," in Infectious Disease Informatics, New York, NY: *Springer New York*, 2010, pp. 223–244. doi: 10.1007/978-1-4419-1327-2_11.
59. U. G. K. Srikanth et al., "Evaluation of Safety and Potency of Kyasanur Forest Disease (KFD) Vaccine Inactivated with Different Concentrations of Formalin and Comparative Evaluation of In Vitro and In Vivo Methods of Virus Titration in KFD Vaccine.," *Biomedicines*, vol. 11, no. 7, Jun. 2023, doi: 10.3390/biomedicines11071871.
60. B. Bohra, K. S. Srivastava, A. Raj, N. Pal, and R. Shukla, "Kyasanur Forest Disease Virus: Epidemiological Insights, Pathogenesis, Therapeutic Strategies, and Advances in Vaccines and Diagnostics," Aug. 01, 2025, Multidisciplinary Digital Publishing Institute (*MDPI*). doi: 10.3390/v17081022.