Forest loss shapes the landscape suitability of Kyasanur Forest disease in the biodiversity hotspots of the Western Ghats, India.

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Abstract

Background: Anthropogenic pressure in biodiversity hotspots is increasingly recognised as a major driver of the spillover and expansion of zoonotic disease. In the Western Ghats region of India, a devastating tick-borne zoonosis, Kyasanur Forest disease (KFD), has been expanding rapidly beyond its endemic range in recent decades. While it has been suggested that anthropogenic pressure in the form of land use changes that lead to the loss of native forest may be directly contributing to the expanding range of KFD, clear evidence has not yet established the association between forest loss and KFD risk.

Methods: The current study sought to investigate the relationship between KFD landscape suitability and both forest loss and mammalian species richness to inform its epidemiology and infection ecology. Forty-seven outbreaks of KFD between 1 January, 2012 and 30 June, 2019 were modelled as an inhomogeneous Poisson process.

Results: Both forest loss (relative risk (RR) = 1.83; 95% C.I. 1.33 – 2.51) and mammalian species richness (RR = 1.29; 95% C.I. 1.16 – 1.42) were strongly associated with increased risk of KFD and dominated its landscape suitability.

Conclusions: These results provide the first evidence of a clear association between increasing forest loss and risk for KFD. Moreover, the findings also highlight the importance of forest loss in areas of high biodiversity. Therefore, this evidence provides strong support for integrative approaches to public health that incorporate conservation strategies simultaneously protective of humans, animals, and the environment.

Key Words: Kyasanur Forest Disease, landscape epidemiology, deforestation, zoonoses, Western Ghats, tick-borne disease

Key Messages

* Deforestation was associated with the risk of Kyasanur Forest disease, a severe tick-borne disease in South India.
* Disease risk was also concentrated in areas of high biodiversity in one of the world’s most important biodiversity hotspots.
* These findings suggest the potential benefit of leveraging conservation efforts in the service of public health

Introduction

Kyasanur Forest disease (KFD), or ‘monkey fever’, is one of India's impactful and long-neglected tick-borne infections, causing approximately 400-500 human cases annually in the Western Ghats region of the country's southwestern states. The disease manifests as flu-like illness followed by potential haemorrhagic and neurologic sequelae; case fatality ranges between 2-10% (1,2). Named after the Kyasanur Forest area in the Shimoga District of Karnataka where the disease was first identified in 1957, KFD has expanded extensively over the last twenty years beyond its early endemic range and now exhibits higher and more widespread incidence across the region(1,3). Due to the relatively high morbidity and mortality in humans, and devastating impacts on local monkey populations (particularly bonnet macaques, *Macaca radiata*, and gray langurs, *Semnopithecus entellus*)(1,3), the rapid expansion of KFD is cause for considerable concern. Once a focus of prominent early research, KFD initiatives diminished by the early 1970s when national research bodies withdrew support leaving the provincial state to manage the disease in the relatively small geographical area in and around Shimoga district. Because of the lack of concerted epidemiological investigation in the succeeding decades, despite regular annual outbreaks of disease, the epidemiology and infection ecology of KFD remain elusive, as is an effective intervention.

Kyasanur Forest disease is caused by the Flavivirus, Kyasanur Forest disease virus (KFDV), and transmitted by several tick species. However, the forest tick, *Haemaphysalis spinigera*, has been consistently identified as the most important vector due to its high relative abundance, high viral prevalence, and its affinity for both humans and other non-human mammals(4–6). Human incidence exhibits a marked seasonality with new cases typically occurring between December and May, corresponding to most of the Western Ghats’ dry season and up to the time just prior to the onset of the monsoons(7). Consistent with the expanded geographic range, the disease now exhibits some seasonal variation in relation to the varied timing of the rainy season in the five states in which it is reported.

The seasonality of KFD is driven by the seasonality of the tick vectors, particularly the nymphal stage, which is most abundant from December through March and often persists up to June(6). *H. spinigera* exhibits a typical hard tick 3-host life cycle (Figure 1) (6,8,9). Throughout the tick’s life cycle there is little to no vector transmission between humans(1). In addition to transstadial and transovarial viral infection in ticks (Figure 1), uninfected ticks can also be infected by their vertebrate hosts. Cattle have been shown to be sero-reactive to KFDV, but they generally show low susceptibility to infection(10). Definitive wildlife reservoirs for KFDV have not been identified, although susceptibility has been reported in several vertebrate hosts(3). Monkeys suffer high mortality during epizootics, and are, like humans, considered incidental hosts rather than reservoirs(11–13). The virus has been identified in other mammalian species, particularly rodents(14–20) and bats(21–25), but definitive maintenance hosts have not been adequately delineated. Nevertheless, foci of KFD spillover to humans do appear to be coincident with areas of higher mammalian species richness in the biodiversity hotspots of the Western Ghats(26,27). These areas may be especially vulnerable to human perturbation via deforestation and other forms of changing land use throughout the region.

It has been suggested that the expansion of the range of KFD in recent decades is the direct result of the loss of forest habitat(1,28). The Bandipur Forest range from Maharashtra to Kerala and Tamil Nadu has seen many forest lands transformed for agricultural purposes over the last few decades, with many tribal and forest villagers displaced from their original homelands and onto deforested land. Often these displaced people are resettled within or on the periphery of new agricultural development, including commercial plantations of areca nut or cashew. These changes may induce consequent changes in the landscape epidemiology of KFD by way of novel interactions between wildlife and humans and their shared ticks. However, this has not yet been formally investigated.

The current study seeks to locate and describe the landscape suitability of KFD in the Western Ghats states of South India by modelling the spatial dependence of KFD occurrence as a function of environmental landscape features across the region. Secondarily, this study aims to infer relationships between KFD and specific landscape features to inform the epidemiology and infection ecology of this zoonosis as an aid toward developing interventions for the mutual benefit of human, animal, and ecosystem health. It was hypothesised that increasing forest loss would be directly associated with an increase in KFD across the region.

Methods

Data sources

Forty-seven outbreaks of KFD were identified from the ProMED-mail electronic surveillance system between 1 January, 2012 and 30 June, 2019. This is an electronic surveillance service provided by the International Society of Infectious Diseases comprising formal and informal reports of infectious disease occurrences. The daily reports undergo screening by a multinational team of editors, moderators, and country managers, who systematically evaluate incoming reports and, when necessary, engage the extensive body of locally-sourced subscribers to elicit their unique and experienced insight to support or refute alerts (29). Data captured by ProMED-mail thus do not represent a population-based sample but are instead a more limited cross-section of disease experience. However, we did validate the ProMED-mail data by evaluating model performance using an independent sample of 39 laboratory-confirmed KFD outbreaks over a similar period (1 January, 2014 to 30 June 2019) as reported separately in the scientific literature(26,30–32). This latter evaluation (see statistical methods below) thus provides an externally validated assessment of the modelled KFD suitability, and only the second such validation of ProMED-mail surveillance data in India(33). The distribution of ProMED-mail KFD outbreaks across the Western Ghats states from 1 January, 2012 to 30 June, 2019 is presented in Figure 2, superimposed over the kernel density estimate. All reported outbreaks were recorded at a spatial resolution of at least 5 km.

The WorldClim Global Climate database(34) was used to capture aggregate spatio-temporal weather station data between 1950 and 2000, which were extracted at a resolution of 30 arc seconds. The metrics derived from this database are mean measurements between 1950 and 2000, and thus represent climate estimates over time. While there can be some global regions that have sparse representation of weather stations contributing to this data product, India is well represented with an extensive network of weather stations having contributed to this decadal climate interpolation (35). Because KFD is highly influenced by the dry season, mean dry quarter precipitation and mean dry quarter temperature were used for this investigation rather than mean annual aggregates alone(3). Moisture is also important to tick behaviour, exerting significant pressure on the time ticks can sustain questing(6,8). Therefore, in addition to the KFD season-specific measure of precipitation, an annual measure of precipitation was also included to reflect year-round moisture availability. We note that the correlation between these two measures of precipitation was very low (Pearson’s *r* = 0.09).

The Database of Global Administrative Areas was used to obtain shapefiles for the surface water and waterways across the region [gadm.org]. Forest loss was determined using the 30-meter resolution Landsat data compiled by the Global Forest Change project(36), and represented forest lost between 2000 and 2012. This data product is based on processed Landsat imagery using a stratified random sampling validation procedure, the overall accuracy of which was determined to be 99.6% or 99.5% in global and tropical settings, respectively(36). A new raster was generated from this data product to represent deciles of forest loss. Finally, a 30 arc-second raster of mammalian species richness (number of species per ~ 1 km2) was acquired from the Socioeconomic Data and Applications Center (SEDAC) repository(37). This data product is derived from the geographic extent of all mammal species (5,488 species in 156 families) as assessed by the International Union for the Conservation of Nature, and compiled by the Center for International Earth Science Information Network at Columbia University. Mammalian species richness was used as a proxy for mammalian ɣ-diversity in the Western Ghats region. The aim was to delineate biodiversity hotspots rather than attempt to explore the influence of specific taxonomic groups, such as rodents or bats, or individual species on KFD suitability.

Statistical Analysis

The kernel density estimate of KFD outbreaks applied an isotropic Gaussian function for the kernel with normal reference bandwidth(38). The KFD outbreaks were modelled as a point process(39). This approach allows the evaluation of the distribution of outbreaks as spatially dependent and can investigate such dependencies with respect to environmental features.

First, outbreaks were evaluated as a homogeneous Poisson process with conditional intensity,

 λ(u,X) = β (1)

where u represents the set of locations corresponding to KFD outbreaks, X, and β is the intensity parameter. This served as the null model of complete spatial randomness. Under this model, the expected intensity (i.e. number of points in a specified subregion of the X window) is simply proportional to the area of the subregion under consideration(39).

Second, this null model was then compared to an inhomogeneous Poisson process, which delineates spatial dependency in KFD outbreaks and has conditional intensity,

 λ(u,X) = β(u) (2)

This model formulates the intensity as a function of the location, u, of the points (KFD outbreaks). Both the markedly better fit of the inhomogeneous Poisson process and the significant divergence of the K-function (see Results) suggested that the intensity of KFD outbreaks was spatially dependent and therefore a spatially explicit model to describe their occurrence was considered most appropriate. Thirteen separate inhomogeneous point process models with environmental covariates (described below) were fitted with conditional intensity,

 λ(u,X) = ρ (Z(u)) (3)

where ρ is the function describing the association between the point intensity and the covariate Z at location u. Mean dry quarter precipitation, mean dry quarter temperature, mean annual precipitation, proximity to waterways, surface water presence, deciles of forest loss, and mammalian species richness were the covariates included in the inhomogenous Poisson models described above (Figure S1). These covariates were aggregated to scales of 2.5 and 10 arc minutes, respectively, for the two spatial scales under evaluation. The correlation among all covariates under consideration was low (all values of the Pearson’s *r* were < 0.5). The association between the KFD outbreak intensity and each covariate was quantified with the relative risk derived from the regression coefficients of the inhomogeneous Poisson models. Additionally, we included the 2010 population density as an offset in the models so that predicted landscape suitability could correctly represent epidemiological risk. Model fit was assessed using the Akaike information criterion (AIC) and model performance assessed using the area under the receiver operating characteristic curve (AUC) using the independent, laboratory-confirmed testing dataset of KFD outbreaks. As such, the models were trained using the ProMED-mail data and tested using the independent data so that the AUCs reflect externally-validated model performance. Among the 13 models considered, the best model was selected based on performance and fit using the AUC and AIC, respectively.

All models were evaluated at fine (2.5 arc-minutes) and coarse (10 arc-minutes) scale to determine if the modelled suitability was robust to scale since the influence of biotic (mammalian species richness) and abiotic features (all others) on infectious disease processes have been shown to vary differentially with respect to spatial scale(40). This sensitivity analysis evaluated scale dependence across all models with respect to model fit (AIC) and performance (AUC). K-functions were fitted to the KFD outbreaks to identify spatial dependencies before and after the point process was modelled as a function of the landscape features to determine if these features sufficiently explained the spatial dependence. All analyses were performed using R statistical software version 3.6.0(41). The kde.points function in the GISTools package was used to estimate the kernel function(42). The ppm function in the spatstat package was used for the point process models and the envelope function in the same package used for estimating the K-functions(43,44). The silhouette images depicting tick host taxons in Figure 1 were obtained from phylopic.org and used under Creative Commons license. Tick images in Figure 1 were created by the authors.

Results

The best model of KFD landscape suitability was selected based on optimal fit and performance from among all models considered (Model 4, Table S1) and is presented in Table 1. According to this model, and indeed all models in which they were included (Table S1), the most impactful features to KFD suitability were forest loss (RR = 1.83; 95% C.I. 1.33-2.51) and mammalian species richness (RR = 1.29; 95% C.I. 1.16-1.42), whereby each decile increase in forest loss corresponded to an 83% increase in KFD outbreak risk and each species increase in mammalian richness corresponded to a 29% increase in risk. Moreover, it appeared that forest loss and species richness were not representing the same landscape phenomenon in their associations with KFD (Table S1); both the AIC and AUC were better for forest loss alone (Model 11) than for mammalian richness alone (Model 12), but the fit and performance were better still in the model with both forest loss and mammalian richness (Model 13). The dry quarter temperature was also positively associated with KFD outbreaks with each degree increase in mean temperature during the dry season associated with a 33% increase in risk (RR = 1.33; 95% C.I. 1.03-1.72). Interestingly, although precipitation fit and performed better than temperature in the climate models (Models 9 and 10 in Table S1), precipitation was no longer significantly associated with KFD outbreaks in the final model. The models were largely invariant to scale at the two scales examined here, which was reflected in both the relative parameter estimates of each landscape feature as well as the relative model fit and performance.

(Table 1 here)

The predicted KFD suitability based on the final model is presented in the middle panel of Figure 3, with the lower and upper 95% confidence limits presented to the left and right, respectively. A well-defined corridor encompassing the region of the Western Ghats and its fringes transects the full extent of western Karnataka and extends from there into Goa and southern Maharashtra to the north, and northeastern Kerala and northwestern Tamil Nadu in the south. In addition, there is fragmented, yet notable, increased suitability along the tri-state border areas of Karnataka, Kerala, and Tamil Nadu. As described above, predicted KFD suitability was largely scale invariant (Figure S2).

The strong spatial dependency of KFD outbreaks identified in the homogenous K-function (left panel, Figure 4) was adequately accounted for by the fitted inhomogenous Poisson model as is shown in the right panel of Figure 4, wherein the empirical and theoretical (under spatial randomness) functions no longer diverge across most of the function. The same was true for the model assessed at coarser spatial scale (Figure S3).

Discussion

We present the first study to specifically examine the impact of forest loss on the expansion of KFD beyond its endemic range and have consequently identified deforestation as a dominant feature delineating the landscape suitability of this devastating tick-borne infection. In addition, the association between increased KFD and species richness conjointly with forest loss suggests that increasing anthropogenic pressure on wildlife habitat may be inadvertently increasing human exposure to KFD reservoirs and their tick vectors. This finding highlights the potential for conservation of forested areas as a fruitful public health intervention with positive downstream benefits for the humans, animals, and ecosystems inhabiting the Western Ghats.

Increases in KFD outbreaks associated with deforestation have been described anecdotally, and excellent epidemiological arguments have been made regarding the potential influence of forest loss on increasing spillover of KFD to humans(3,28). However, the spatial distribution of the expanded range of KFD has not previously been interrogated specifically with respect to forest loss across the region of the Western Ghats. Forest degradation in the region has been recognized for some time. A landmark study in 2000 by Jha and colleagues reported a loss of native forest greater than 25% over the two decades between 1973 and 1995(45). While deforestation may have slowed more recently, it has by no means been arrested as indicated by the forest loss described in the current study, which remained as high as 12% in some locales (Figure S1). Data describing the risk of tick exposure among humans in fragmented tropical forests in the Western Ghats is currently lacking, however forest fragmentation in temperate regions has been associated with substantially increased risk of tick encounters and human infection with tick-borne disease(46–49). More importantly, high abundance of *H.* *spinigera* and KFDV prevalence in these ticks has consistently been identified in the affected forested areas in the Western Ghats(4,5), so the current findings are not surprising. Moreover, some evidence has shown ticks moving from forest forage and adapting to peri-domestic shrubs and medium height agricultural products, such as are found in cashew plantations(4). Nevertheless, these results are not posited as definitive and will require further validation from more targeted fieldwork linking tick surveys with wildlife and human serosurveys in forest fringe areas of the Western Ghats.

This study also found a strong association between KFD landscape suitability and mammalian species richness, wherein higher biodiversity was associated with increased risk. In 2000, at the beginning of the period of the current study, the Western Ghats was recognized as one of the top eight "hottest hotspots" of biodiversity on the planet(50). The Western Ghats region was subsequently added as a UNESCO World Heritage site in 2012(51). The emergence of anthropogenic ecotones in such a biologically diverse region presents ample opportunity for interaction between humans and forest wildlife, as well as the sharing of disease vectors. Susceptibility to KFDV infection has been noted in several mammalian species. As noted previously, the bonnet macaque and gray langur are both susceptible to infection and are often severely affected by the disease, but the high mortality attending epizootics in these species limits their contribution to viral maintenance(11–13). In addition, evidence of infection has also been established in several rodent species(14–20) and bat species (21–25). However, virus isolation was limited to only two of these species, so their competence for the virus is unknown as is their capacity to act as maintenance or amplifying hosts. Exploration of the role of individual species was beyond the scope or capacity of the current study.

Because this investigation did not observe community-level interspecific interaction, we cannot make any claims against or in favour of specific ecological phenomena such as amplification or dilution effects(52). The associations between KFD and both forest loss and species richness do, however, suggest that anthropogenic pressure operating in one of the world's most important biodiversity hotspots could be contributing to the expansion of this important disease. This is supported by recent work showing fragmentation of habitat in areas of high biodiversity as a key driver of pathogen spillover to humans(53), and other work showing the influence of land conversion on interspecific interaction, human contact patterns with wildlife, and spillover(54). In addition, despite the inability to delineate amplification or dilution effects in KFD transmission from the current study, preserving biodiversity has been shown to be generally protective against spillover of zoonotic pathogens to humans regardless of whether dilution or amplification dominates among wildlife transmission for any particular pathogen system(55). As such, renewed efforts in conservation of the forests of the Western Ghats and the protection of their resident wildlife could be leveraged toward potentially impactful and long-term public health initiatives.

The importance of the availability of moisture in the landscape to the life cycle of *Haemaphysalis* ticks is well documented(6). Therefore, this study was careful to consider both annual and seasonally-specific precipitation as well as the presence of water in the landscape, measured by both its surface water and the flow of water through it. Interestingly, none of these proved particularly impactful to KFD suitability. Moreover, even though precipitation demonstrated a substantially greater influence on KFD suitability than temperature when only climatic factors were evaluated (S2 Table 1), when forest loss and species richness were accounted for this was no longer the case. An association with temperature did remain, however. A definitive explanation for this finding cannot be proffered, however it may be that the very high degree of precipitation that falls across the whole region during the monsoon season results in relatively homogenous water presence in the landscape. As a result, temperature variance may be more influential to relative humidity across the region during the dry season and thus could emerge as a more significant climatic factor. Alternatively, some epidemiologists still consider forest visitation, which is far more common in the dry season, as a critical risk factor for cases of KFD in humans in Wayanad and Karnataka states(5,26). It is important to note, however, that if warmer climatic temperature is associated with increased KFD suitability the current trend in global warming, which may be exacerbated locally by deforestation(56), could exert further influence on the expansion of this tick-borne zoonosis. As such, we would recommend more localised and detailed measurement of climate in future investigations of KFD.

There are several limitations attending this study. First, as described above, ProMED-mail surveillance provided the source of KFD outbreak data used to train the models that served as the basis for this investigation. We acknowledge that this system may not have identified all KFD outbreaks due to variability in the quality of reporting infrastructure across the states inclusive of the Western Ghats. However, we did test the fitted models against an independent laboratory-confirmed sample of KFD outbreaks to provide external validation of the findings, and a previous study of a different zoonotic disease validated ProMED-mail data in India using a similar approach(33). Nevertheless, we recognize that the data may not be representative of all KFD occurrence across the Western Ghats and that there may be some bias toward larger outbreaks. Second, the scale of the study is coarse following from the limited scale of reporting of the ProMED-mail system. While this is unlikely to be of substantial influence to abiotic environmental features which are expected to dominate at coarse spatial scale, it may be influential to biotic features which are expected to dominate at fine scale(40). Third, the climate features were based on averages from the period 1950 to 2000, which therefore assumes temporal homogeneity of precipitation and temperature over that period as well as over the duration of KFD outbreak observation in the current study.

In conclusion, this study provides the first concrete evidence for the impact of deforestation on the expanded risk of one of India's most important emerging vector-borne diseases. These findings suggest that interventions targeting conservation of forest and wildlife may yield substantial public health benefits for communities living in emergent forest fringe ecotones. This work also contributes to a growing body of evidence that identifies the loss of natural habitat and the subsequent perturbation of wildlife populations and their vectors as key drivers of zoonotic disease transmission(57,58). This emerging global pattern of spillover risk has profound implications for how we respond to, control, and ultimately prevent emerging infectious diseases. The One Health paradigm, which advocates for the collective promotion of human, animal, and environmental health, offers a viable framework for developing solutions to the problem of disease emergence at the wildlife-human interface. The benefits of transdisciplinary disease surveillance and cross-training of practitioners associated with One Health initiatives have been well-demonstrated in resource-poor tropical settings for other arboviruses exhibiting complex ecology(59). A One Health approach that simultaneously incorporates the experience and practice of human, veterinary, and forest department services and scientific research could be expected to generate similar success for KFD in the Western Ghats.

Table 1. Adjusted relative risks and 95% confidence intervals for the associations between Kyasanur Forest disease outbreaks in humans and each landscape feature. The relative risks are derived from an inhomogeneous Poisson model of the point process. Each landscape factor is adjusted for all others.

|  |  |  |  |
| --- | --- | --- | --- |
| Landscape features | Relative Risk | 95% Confidence Interval | p-value |
| Forest loss (deciles) | 1.83 | 1.33 – 2.51 | 0.0001 |
| Mammal species richness (# species) | 1.29 | 1.16 – 1.42 | 0.0001 |
| Annual precipitation (cm) | 1.00005 | 0.997 – 1.0004 | 0.76 |
| Dry quarter precipitation (mm) | 0.96 | 0.92 – 1.01 | 0.09 |
| Dry quarter temperature (Celsius) | 1.33 | 1.03 – 1.72 | 0.01 |

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